CODING FORM FOR SRC INDEXING REVISED 10/15/86

Microfiche No.
OTS0515144

New Doc I.D.
86-870000617

Old Doc I.D.

Date Produced
8/25/80

Date Recieved
7/27/87

TSCA section
8D

Submitting Organization
INTL ISOCYANATE INST

Contractor
BAYER AG

Document Title
GENERATION AND MONITORING OF BREATHABLE AEROSOLS OF DIPHENYL METHANE DIISOCYANATE WITH ATTACHMENTS AND COVER LETTER DATED 072287

Chemical Category
DIPHENYL METHANE DIISOCYANATE (101-68-8)

INTERNATIONAL ISOCYANATE INSTITUTE, INC.
119 CHERRY HILL ROAD
PARSIPPANY, NEW JERSEY 07054

TELEX 383600

CONTAINS NO CBI

(201) 263-7517

22 July 1987

86-870000617

Document Processing Center (TS-790)
Office of Toxic Substances
Environmental Protection Agency
401 M Street, S.W.
Washington, D. C. 20460

Attention: 8(d) HEALTH and SAFETY REPORTING RULE (REPORTING)
May 1, 1987

Dear Sir or Madam:

As described at 40 C.F.R. 716.20(a) (10), the International Isocyanate Institute (III) submits the enclosed studies on behalf of its members to satisfy member reporting requirements under Section 8(d) of the Toxic Substances Control Act. These studies are on chemicals added to the 8(d) list on May 1, 1987. The studies are indexed by CAS numbers with chemical name, III identification number and title provided.

Attachment #1 is an indexed list of completed studies.

Attachment #2 is a compilation of the reports from the completed studies.

Attachment #3 is an indexed list of studies that are currently in progress.

Please refer to the III identification number in any communication regarding the report.

If the Agency needs further information, please do not hesitate to contact me.

Very truly yours,

R. K. Rigger
Managing Director

RKR/c
enclosures

86-870000617

ATTACHMENT #1

INDEXED LIST OF COMPLETED STUDIES

CAS # 101-68-8 Benzene, 1,1'-methylenebis[4-isocyanato-
Methylenedi-p-phenylene diisocyanate
4,4'-Methylenebis(phenyl isocyanate)
MDI
4,4'-Diisocyanatodiphenylmethane

III NUMBER	TITLE
10000	Prepolymeric MDI (Biphenylmethane Diisocyanat) with and without added Phenyl Isocyanate (PhI) - one hour acute inhalation toxicity.
10005	Determination of the concentration of vapor generated from monomeric 4,4'-Diphenylmethane Diisocyanate (MDI) by a dynamic method.
10008	Two-day study into the relation between polymeric MDI concentration values obtained by a QCM-Cascade, HPLC and Colorimetry.
10010	Liquid Waste after TDI/MDI decontamination.
10012	Literature Study on Reaction of Isocyanates with Biological Materials.
10013	Report on fire hazard of Isocyanate chemicals.
10014	Report on fire hazard of Isocyanate chemicals.
10018	Analytical methods to monitor aerosols of Polymeric 4,4'-Diphenylmethane-diisocyanate (MDI) at low concentrations.
10019	Aquatic life study phase II, step 2 Accumulation of TDI, MDI, TDA and MDA in fish and their toxicity.
10022	Generation and monitoring of breathable aerosols of polymeric 4,4'-diphenylmethane-diisocyanate (MDI).

ATTACHMENT #1

INDEXED LIST OF COMPLETED STUDIES

CAS #101-68-8 Benzene, 1,1'-methylenebis[4-isocyanato-
Methylenedi-p-phenylene diisocyanate
4,4'-Methylenebis(phenyl isocyanate)
MDI
4,4'-Diisocyanatodiphenylmethane

III NUMBER	TITLE
10026	Pre-polymeric diphenylmethane,4,4', diisocyanate (Petmar MDI) Pre-polymeric diphenylmethane,4,4', diisocyanate + phenyl isocyanate. 50 ppm. Pre-polymeric diphenylmethane,4,4', diisocyanate + phenyl isocyanate. 150 ppm. An experiment to investigate the relative sub-acute toxicity of the above substances in the rat by inhalation.
10050	Metabolism and toxicogenetics of Methylenedianiline.
10065	A study of the diffusion of MDI in rats contaminated via the respiratory system.
10074	Investigations on the microbial degradation of PU forams. Part II.
10075	Respiratory Sensitivity Study.
10076	Deposition of aerosol components on the hair of rats exposed to polymeric MDI aerosols.
10077	Acute inhalation toxicity study of polymeric MDI in rats.
10092	Biological action of TDI and MDI in water.
10129	Immunological aspects of Isocyanates.
10187	Isocyanates : Irritation and Hypersensitivity.
10188	Preliminary study on skin sensitization caused by MDI solutions.

ATTACHMENT #1

INDEXED LIST OF COMPLETED STUDIES

CAS # 101-68-8 Benzene, 1,1'-methylenebis[4-isocyanato-
Methylenedi-p-phenylene diisocyanate
4,4'-Methylenebis(phenyl isocyanate)
MDI
4,4'-Diisocyanatodiphenylmethane

III NUMBER	TITLE
10206	Aquatic life study Phase II, Step 2, Accumulation of TDI, MDI and their reaction products in Daphnia.
10223	TDI and MDI immunological studies. Summary report of research supported by the International Isocyanate Institute.
10234	Aquatic life study Phase II, Step 1. Biodegradation of TDI and MDI in the model river and marine water.
10243	Mortality among workers exposed to isocyanates. Feasibility Study.
10253	Sub-chronic (13 week) inhalation toxicity study of polymeric MDI aerosol in rats (part B2)
10258	Ecotoxicity of Toluenediisocyanate (TDI) Diphenylmethanediisocyanate (MDI) Toluenediamine (TDA) Diphenylmethanediamine (MDA)
10299	Aquatic Life Studies
10317	Production and control of breathable MDI aerosols for primal experiments.

ATTACHMENT #1

INDEXED LIST OF COMPLETED STUDIES

CAS # 101-68-8 Benzene, 1,1'-methylenebis[4-isocyanato-
Methylenedi-p-phenylene diisocyanate
4,4'-Methylenebis(phenyl isocyanate)
MDI
4,4'-Diisocyanatodiphenylmethane

III NUMBER	TITLE
10360	Generation of 4,4' Diphenylmethane Diisocyanate (MDI) vapour
10386	Pharmacokinetics of MDI after inhalation exposure of rats to labelled MDI.
10391	Skin sensitization by isocyanates.
10393	Study of the burning characteristics of isocyanate chemicals.
10439	Di-Isocyanate Induced Asthma - Reactions to TDI, MDI, HDI and Hisamine.
24298	Acute Inhalation Toxicity (LC_{50}) in the Male Albino Rat.

ATTACHMENT #1

INDEXED LIST OF COMPLETED STUDIES

CAS #1321-38-6 Benzene, diisocyanatomethyl-(unspecified isomer)

III NUMBER	TITLE
10010	Liquid waste after TDI/MDI decontamination.
10012	Literature Study on Reaction of Isocyanates with Biological Materials.
10013	Report on fire hazard of Isocyanate chemicals.
10014	Report on fire hazard of Isocyanate chemicals.
10019	Aquatic life study phase II, step 2 Accumulation of TDI, MDI, TDA and MDA in fish and their toxicity.
10024	Tolylene di-isocyanate three week inhalation toxicity in the rat.
10033	Stack Emission Part B : Emitted TDI Gas Treatment with Activated Carbon.
10034	Stack Emission Part A : Emitted TDI Gas Treatment with Activated Sludge.
10035	The toxicity and carcinogenicity to rats of Toluene Diisocyanate vapour administered by inhalation for a period of 113 weeks.
10040	Reaction of TDI with water and with wet sand.
10044	Emission of Tolylene Diisocyanate (TDI) and Tolylene Diamine (TDA) in flexible polyurethane foam production lines.
10045	Emission of Tolylene Diisocyanate (TDI) and amines.
10055	Preparation and evaluation of a system for exposing rats to Toluene Diisocyanate vapour.

ATTACHMENT #1

INDEXED LIST OF COMPLETED STUDIES

CAS # 1321-38-6 Benzene, diisocyanatomethyl- (unspecified isomer)

III NUMBER	TITLE
10057	Evaluation of a system for exposing hamsters to Toluene Diisocyanate vapour.
10064	A study of the diffus rate of TDI in rats contaminated via the respiratory system.
10074	Investigations on the microbial degradation of PU foams. Part II
10075	Respiratory sensitivity study.
10089	Studies of Toluene Diisocyanate induced pulmonary disease.
10092	Biological action of TDI and MDI in water.
10094	Foam plant stack emission data.
10095	Stack Emission Part B : Emitted TDI Gas Treatment with Activated Carbon "Regeneration of Spent Activated Carbon".
10096	Stack Emission Part A : Emitted TDI Gas Treatment with Activated Sludge.
10098	Epidemiological study for effects of TDI.
10100	Histopathological observations on selected tissues of syrian hamsters exposed by inhalation to vapors of Toluene Diisocyanate (TDI) for 6 hours/day, 5 days/week for 4 weeks.
10116	Review of the incidence of rhinitis in rats exposed chronically to Toluene Diisocyanate vapour.

ATTACHMENT #1

INDEXED LIST OF COMPLETED STUDIES

CAS # 1321-38-6 Benzene, diisocyanatomethyl- (unspecified isomer)

III NUMBER	TITLE
10117	Review of the national toxicology program carcinogenesis bioassay of Toluene Diisocyanate.
10121	Toluene Diisocyanate (TDI) proposed exposure standard.
10129	Immunological aspects of Isocyanates.
10142	Toluene Diisocyanate acute inhalation toxicity in the rat.
10153	A 30-day repeated inhalation toxicity study of Toluene Diisocyanate (TDI) in laboratory animals.
10159	The fate of Toluene Diisocyanate.
10162	Epidemiological study for effects of TDI.
10163	Validation of MCM 4000 personal monitor and MCM 4100 integrating reader/recorder system.
10168	Summary of work carried out on FE-A-14 III - 1 by H. Sakurai and co-workers.
10169	The toxicity and carcinogenicity to rats of Toluene Diisocyanate vapour administered by inhalation for a period of 113 weeks.
10175	Emission of Tolylene Diisocyanate (TDI) and Tolylene Diamine (TDA) in flexible polyurethane foam production lines.
10184	Immunological studies on TDI exposed workers. Part I.
10187	Isocyanates : Irritation and Hypersensitivity.

ATTACHMENT #1

INDEXED LIST OF COMPLETED STUDIES

CAS # 1321-38-6 Benzene, diisocyanatomethyl- (unspecified isomer)

III NUMBER	TITLE
10206	Aquatic life study Phase II, Step 2, Accumulation of TDI, MDI and their reaction products in Daphnia.
10208	The Toxicity and Carcinogenicity to rats of Toluene Diisocyanate vapour administered by inhalation for a period of 113 weeks. Addendum Report. Vol. 2.
10210	The Toxicity and Carcinogenicity to rats of Toluene Diisocyanate vapour administered by inhalation for a period of 113 weeks. Vol. I
10223	TDI and MDI immunological studies. Summary report of research supported by the International Isocyanate Institute.
10233	The Toxicity and Carcinogenicity to rats of Toluene Diisocyanate vapour administered by inhalation for a period of 113 weeks. Addendum Report Vol. 1
10234	Aquatic life study Phase II, Step 1. Biodegradation of TDI and MDI in the model river and marine water.
10237	Isocyanate monomer in PU foam.
10243	Mortality among workers exposed to isocyanates. Feasibility Study.
10258	Ecotoxicity of Toluenediisocyanate (TDI). Diphenylmethanediisocyanate (MDI) Toluenediamine (TDA). Diphenylmethanediamine (MDA)
10259	Sampling and Analysis of TDI atmospheres at Klinikum Grosshadern, Munich.

ATTACHMENT #1

INDEXED LIST OF COMPLETED STUDIES

CAS # 1321-38-6 Benzene, diisocyanatomethyl- (unspecified isomer)

III NUMBER	TITLE
10299	Aquatic Life Studies.
10307	Studies on the effects of TDI on living animals.
10308	Change of TDI in olive oil.
10321	Improvement in RAST for TDI. Parts A and B.
10340	Audit of the national toxicology program carcinogenesis bioassay of toluene diisocyanate.
10345	Isocyanate spillage control.
10348	Immunological Studies on TDI exposed workers Part II.
10349	Isocyanate hypersensitivity.
10382	The toxicity and carcinogenicity of Toluene Diisocyanate vapour when administered to mice over a period of approximately 2 years. Summary Rep.
10383	The toxicity and carcinogenicity of Toluene Diisocyanate vapour when administered to mice over a period of approximately 2 years.
10391	Skin sensitization by isocyanates.
10393	Study of the burning characteristics of isocyanate chemicals.

ATTACHMENT #1

INDEXED LIST OF COMPLETED STUDIES

CAS #1321-38-6 Benzene, diisocyanatomethyl-(unspecified isomer)

III NUMBER	TITLE
10416	Sampling and analysis of TDI atmospheres at Klinikum Grosshadern, Munich.
10430	Protective effect of drugs on late asthmatic reactions and increased airway responsiveness induced by Toluene Diisocyanate in sensitized subjects.
10433	The reactions of OH radicals with Toluene Diisocyanate, Toluenediamine, and Methylene Dianiline under simulated atmospheric conditions.
10434	Metabolism and disposition of ^{14}C-labeled Toluene Diisocyanate (TDI) following oral and inhalation exposure ; Preliminary studies.
10437	Toluene Diisocyanate-Induced Asthma: Bronchial Provocation and Reactivity Studies.
10438	Toluene Diisocyanate-Induced Asthma: Inhalation Challenge Tests and Bronchial Reactivity Studies.
10439	Di-Isocyanate Induced Asthma- Reactions to TDI, MDI, HDI and Histamine.

ATTACHMENT #1

INDEXED LIST OF COMPLETED STUDIES

CAS # 91-08-07 Benzene, 1,3-diisocyanato-2-methyl
TDI, 2-6-diisocyanate

III NUMBER	TITLE
24207	Disposition of 2,6-Toluene Diisocyanate in Fischer 344 rats

ATTACHMENT #2

COMPILATION OF REPORTS FROM III FILES
(AS INDEXED IN ATTACHMENT #1)

These reports arc in envelopes labeled Attachment #2 and are packaged, along with an envelope, addressed to:

Document Processing Center (TS-790)
Office of Toxic Substances
Environmental Protection Agency
401 M Street, S.W.
Washington, D. C. 20460

Attention: 8(d) HEALTH and SAFETY REPORTING RULE
(REPORTING) May 1, 1987

from:

International Isocyanate Institute, Inc.
119 Cherry Hill Road
Parsippany, New Jersey 07054

containing a transmittal letter for these documents.

ATTACHMENT #3

INDEXED LIST OF STUDIES IN PROGRESS

CAS # 101-68-8 Benzene, 1,1'-methylenebis[4-isocyanato-
Methylenedi-p-phenylene diisocyanate
4,4'-Methylenebis (phenyl isocyanate)
MDI
4,4'-Diisocyanatodiphenylmethane

III NUMBER	TITLE
E-A-8	Study of chronic toxicity and carcinogenicity of polymeric MDI aerosol in rats. Part C Study. Current work authorized to begin June 1985. To study chronic toxicity and carcinogenicity of polymeric MDI aerosol in rats. Data sought - Effect on animal tissues. Our current estimated completion date for this study is the first quarter of 1989. It may be possible to complete this study before 1989; however, it may require more time. CIVO Institution, Tno., Toxicology and Nutrition, Utrechtsewe 848, P.O. Box 306, 3700 A.J. Zeist, The Netherlands.
E-H-44	MDI sampling and analysis at CIVO Current work authorized to begin November 1984. To study consistency/comparability of various methods continuous/discontinuous for determining the composition of atmospheres in Study E-A-8 (Part C) above. Data sought - Analytical data on polymeric MDI aerosol atmospheres. Our current estimated completion date for this study is the first quarter 1989. It may be possible to complete this study before 1989; however, it may require more time. CIVO Institution, Tno., Toxicology and Nutrition, Utrechtsewe 848, P.O. Box 306, 3700 A.J. Zeist, The Netherlands.

ATTACHMENT #3

INDEXED LIST OF STUDIES IN PROGRESS

CAS # 1321-38-6 Benzene, diisocyanatomethyl- (unspecified isomer)

III NUMBER	TITLE
E-B-11	Epidemiological study of workers in U.K. flexible foam industries. Current work authorized to begin Mid 1978. To investigate whether working on flexible PU foam manufacturing plants gives rise to increased expectation of decrements in lung parameters above those due to ageing. Data sought - monitoring of exposed workers' and controls' lung parameters. Monitoring of airborne TDI (and on limited scale of tertiary aliphatic amine) in the workplace. Our current estimated completion date for this study is the first quarter of 1989. It may be possible to complete this study before 1989; however, it may require more time. Tynestead Limited, Tynestead House, 22 Camberley Drive, Bamford, Rochdale, Lancs, OL11 4 AZ, UK. and Medical Research Council, 20 Park Crescent, London, UK.

ATTACHMENT #3

INDEXED LIST OF STUDIES IN PROGRESS

CAS # 1321-38-6 Benzene, diisocyanatomethyl- (unspecified isomer)

III NUMBER	TITLE
FE-AB-14	Epidemiological study of workers in Japan flexible foam industries. Phase V.

Current work authorized to begin August 1985.
To clarify relationship between TDI concentration and chronological change in pulmonary and respiratory symptoms of workers in PU foam plants. Data sought.
Monitoring of exposed workers' and controls' lung parameters.
Monitoring of airborne TDI in the workplace.
Our current estimated completion date for this study is the first quarter of 1989. It may be possible to complete this study before 1989; however, it may require more time.
School of Medicine, Keio University, Shinjuki-Ku, Tokyo, Japan.

ATTACHMENT # 3

INDEXED LIST OF STUDIES IN PROGRESS

CAS # 1321-?8-6 Benzene, diisocyanatomethyl- (unspecified isomer)

III NUMBER	TITLE
E-E-22	Clean Stack Air Project Current work authorized to begin March 1980. To study ways in which TDI Emissions from flexible foam plants can be removed from exhaust gases by carbon absorption. Data sought - Concentrations of TDI at inlets and outlets of carbon absorption units. Our current estimated completion date for this study is the first quarter of 1989. It may be possible to complete this study before 1989; however, it may require more time. Dunlop (Now BTR, Silvertown House, Vincent Square, London, UK.
E-AB-40	An investigation into the mortality and cancer morbidity of production workers in the UK flexible polyurethane foam industry. Current work authorized to begin July 1987. To compare the mortality and cancer morbidity experience of production workers in UK flexible foam manufacturing plants with those of unexposed controls and of the population at large, and to determine, if appropriate, possible reasons for differing experiences. Data sought. Comparative Data on death and illness due to cancer, analysed statistically. Data sought. The expected date of termination of project is indeterminate since it depends on results found at different intervals. The first analysis will take place 1989. Cancer Epidemiology Unit, University of Birmingham, Edgbaston, Birmingham UK.

ATTACHMENT #3

INDEXED LIST OF STUDIES IN PROGRESS

CAS #1321-38-6 Benzene, diisocyanatomethyl- (unspecified isomer)

III NUMBER	TITLE
NA-E-24	Fate of airborn TDI (Part II)

Current work authorized to begin May 1984.
To determine the fate of airborne TDI and the effects of moisture, light, and atmospheric pollutants on TDI loss from the gas phase.
Our current estimated completion date for this study is the first quarter of 1989. It may be possible to complete this study before 1989; however, it may require more time.
Battelle Columbus Laboratories, 505 King Avenue, Columbus, Ohio 43201

NA-AB-26 Detecting delayed isocyanate sensitivity.

Current work authorized to begin May 1, 1987.
This research is being conducted to better detect delayed isocyanate sensitivity in persons exposed and/or sensitized to isocyanates. In 1986, M. Karol's work was directed towards identification of isocyanate-specific lymphocytes by class.
Our current estimated completion date for this study is the first quarter of 1989. It may be possible to complete this study before 1989; however, it may require more time.
Dr. M. Karol, University of Pittsburgh, 130 Desoto Street, Pittsburgh, Pennsylvania 15261

ATTACHMENT #3

INDEXED LIST OF STUDIES IN PROGRESS

CAS #1321-38-6 Benzene, diisocyanatomethyl- (unspecified isomer)

III NUMBER	TITLE
NA-AB-43	Improvement of RAST tests for TDI

Current work authorized to begin May 1, 1987.
This research is being conducted to improve RAST (Radiolabeled Antibody Sorbent Technique) test for identifying exposure and sensitization to TDI. Additional mechanistic work on TDI sensitization is being conducted by Dr Brown. This includes studying proteins in TDI exposed animals.
Our current estimated completion date for this study is the first quarter of 1989. It may be possible to complete this study before 1989; however, it may require more time.
Dr W. E. Brown, Carnegie-Mellon University, Pittsburgh, Pa. 15261.

NA-AB-50 TDI Reprotoxicity

The teratology study was initiated in the 4th quarter of 1986.
The reproduction study was initiated in the 2nd quarter of 1987.
This project evaluates both the "Developmental Toxicity of Inhaled TDI in CD (Sprague-Dawley) Rats" and "Two-Generation Reproduction Toxicity of TDI in CD (Sprague-Dawley) Rats."
Our current estimated completion date for this study is the first quarter of 1989. It may be possible to complete this study before 1989; however, it may require more time.
Dr T. W. Tyl, Bushy Run Research Center, RD #4, Mellon Road, Export, Pennsylvania 15632.

BAYER AG, Leverkusen

GENERATION AND MONITORING OF BREATHABLE AEROSOLS OF POLYMERIC 4,4-DIPHENYLMETHANE-DIISOCYANATE (MDI)

III Project EA 9

Part A: Generation and Physical Monitoring of Breathable Aerosols

Author: Dr. A. Bürkholz, ZB IN-AP VT 1

Part B: Analytical Monitoring

Author: Dr. P. Vogtel, ZB FE-DZA

Co-Authors: Dr. A. Bürkholz
Dr. J. Keller, ZB FE-D

August 25, 1980

List of Contents

Generation and Monitoring of Breathable Aerosols of
Polymeric 4,4 - Diphenylmethane - Diisocyanate (MDI) -
I.I.I.-Project EA 9

Introduction (by Dr. F. Brochhagen)

The International Isocyanate Institute Inc. (I.I.I.) is planning a long term inhalation toxicity study on animals with MDI in order to assess whether this product may present a long term health hazard and whether it may have a carcinogenic potential. Toluene diisocyanate (TDI) is subject of 2 long term I.I.I. sponsored studies of this type since 1975. The test animals in the first investigation were rats; the exposure period was finished by end 1978, the final report will be available in due time. Mice were the test species in the second study which is still going on.

The concentrations chosen for the TDI exposure were 0.05 and 0.15 ppm (≙ 0.35 and 0.105 mg/m^3). These values which are well above the actual TLV (0.02 ppm ≙ 0.14 mg/m^3) were regarded to be low enough not to cause critical acute or subacute toxic effect on the test animals. The doses on the other hand were considered to be sufficiently high to demonstrate long term effects others than those known to the present which have been gained from the increasing handling of TDI over the last 30 years.

The realtively high vapor pressure of TDI allows the vaporisation of the product by heating in order to obtain the concentrations mentioned above. MDI on the other hand due to its low vapor pressure only allows a maximum vapor concentration (at room temperature) of 0.06 - 0.09 ppm ≙ 0.6 - 0.8 mg/m^3 to be produced. It is obvious that this level (Concentration of saturated vapor) can only be obtained under favorable and carefully controlled circumstances.

It has to be assumed that the concentration to be chosen for the long term MDI-study will be of the same order as for TDI. It is therefore necessary to produce a concentration above the saturation point by atomizing the MDI to particles which are breathable (0.3 - 3.0 µm diameter).

Care must be taken that the concentration of MDI in this form is in the order of 1 mg/m^3.

The LC 5o data must be known in order to establish the parameters of a long term inhalation study. It has to be expected that the concentration of MDI to produce an LC 5o 1 h value is in the order of 3oo mg/m^3. A breathable aerosol of this concentration has therefore to be provided also.

A research proposal by Bayer AG dated March 1,1979 outlines the various steps to be made to fulfil these tasks. The proposal became subject of the I.I.I. project EA 9 - MDI Aerosol generation dated Aug. 9,1979.

The following report describes the outcome of this investigation. Part A (Author Dr. A. Bürkholz, ZB IN - AP VT 1) describes the generation and the physical monitoring of the aerosols. Part B (Author Dr. P.Vogtel, ZB FE - DZA Analytik, Co-authors Dr. A. Bürkholz and Dr. J. Keller) presents the data which resulted from the analytical monitoring.

As can be seen from the reports the aerosol generation work was concentrated on polymeric MDI (liquid at room temperature). The analytical monitoring was focussed on the aerosols in the low concentration region which was considered to be of primary importance.

It is to be mentioned that many unexpected implications and difficulties prolonged the duration of the study. This also lead to a considerable increase of the cost in relation to the budgeted sum.

Summary

Generation and Monitoring of Breathable Aerosols of Polymeric 4.4 - Diphenylmethane - Diisocyanate (MDI)

Report Part A: Generation and Physical Monitoring of Aerosols.

Preliminary experiments were carried out using a substitute liquid having atomizing properties very similar to those of polymeric MDI (Desmodur 44 V 20, Bayer AG). Due to the health hazards to be expected on MDI aerosols, an open-air facility was specially constructed for the implementation of the experiments with this product. During these studies the waste air was cleared from aerosol particles to a large extent by means of a highly efficient filter prior to being discharged into the atmosphere.

Two-component nozzles using air or nitrogen as the propellent proved the most suitable for generating aerosols from liquid substances. However, different generator types must be used for high and low concentrations. Concentrations of 1 mg/m^3 can be achieved with a variety of inhalation atomizing nozzles with narrow bores for liquid and propellant. Two or three type 970 nozzles made by the Schlick company have to be combined for generating concentrations of 300 mg/m^3.

Separation of the coarse particles ($> 3\,\mu m$) can be accomplished with the aid of specially designed cyclones. It proved unnecessary to treat the entire airflow of 300 m^3/h. The cyclones can be rather positioned directly downstream of the atomizer nozzle, thus permitting a combination to form a single unit. The amount and fineness of the aerosol depend not only on generator design but also on the pressures of the propellant and the liquid. The temperature of the liquid and the atomizing nozzles has an influence also.

The cyclone type and the air throughput are factors which determine the separation of coarse particles. The necessary atomizing and

separating conditions had to be determined by means of an appropriate series of tests.

Experience was gained on maximum atomization duration for the MDI of approximately 4 hours for the low concentrations, and approximately 15 minutes for the high concentrations. Correspondingly larger supply tanks will have to be provided at a later date for extended atomizing periods.

Monitoring of the aerosol, i.e. measuring its fineness, its particle size distribution and its concentration, was accomplished with the aid of a cascade impactor. This instrument permits the aerosol to be fractionated by sizes, collected on small glass plates and subsequently weighed on a semimicro balance.

Scattered light measuring equipment is most suitable as monitoring equipment for long-term experiments. Of the three equipment types tested the Royco 225 unit proved to be the best, having the capability of instantaneously and reliably indicating any malfunction or change in aerosol generation.

The analytical monitoring of the aerosols after collection by means of cascade impactor, was performed by gravimetric analysis.

The residence time of the aerosols in the inhalation chamber to be used later in the long term inhalation study was simulated by a residence chamber of similar dimensions. Physical monitoring at the entry and the exit of this chamber confirmed that during the residence period (approx. 10 min.) no physical change occurs on the aerosols.

Summary

Generation and Monitoring of Breathable Aerosols of Polymeric 4,4 - Diphenylmethane - Diisocyanate (MDI)

Report Part B: Analytical Monitoring of Aerosols

The sampling for the analytical monitoring of the concentration and of the chemical stability of the generated MDI aerosols was done by collection with the cascade impactor and in conventional manner with impinger-washing-bottles, evacuated gas-pipettes and glass-sintered G4-filters.

The evaluation after collecting with the cascade-impactor was done physically by weighing the deposited masses and analytically by dissolving them in CCl_4 followed by quantitative IR-Spectroscopy. Additional assurance was gained by determination of the TOC-value (total organic carbon value) of the deposited masses by combustion. At intermediate concentrations (5-5o mg/m^3) analytical values lie 2o % below gravimetric values with the difference augmenting to 5o % at low concentrations (<5 mg/m^3). The reasons for these differences were studied and discussed. Within the so given range of error the cascade impactor may be used at intermediate and low concentrations to monitor the aerosol concentration. However this is related to a considerable expense in work and time.

The effectiviness of the direct sampling methods was satisfactory only at the intermediate concentrations. At low concentrations it fell down to 1o - 2o %. The reasons of this were discussed. It is possible that they are caused by a shifting of the center of gravity of the particle size distribution from about 1.6 µm at intermediate concentrations to about o.8 µm at low concentrations.

An independent comparison of the results obtained by measurements with the cascade impactor to those obtained by direct sampling is only possible at intermediate concentrations. For the same reasons no reliable and fast direct analytical method for monitoring the 1 mg range is available at the moment.

The chemical stability of the aerosol was studied at the entry and the exit of the residence chamber at intermediate concentrations. By direct

sampling followed by exclusion chromatography (GPC), thin layer chromatography (TLC) and high performance liquid chromatography (HPLC) after derivatisation of the Isocyanate groups with N-4-nitro-benzyl -N-propylamine and IR-spectroscopy, completed by special tests on formation of aromatic amines and PhI enrichment in the athmosphere, no change between original MDI, the portion separated in the cyclone and the aerosol could be observed. Therefore it can be concluded that no chemical change of the aerosol occurs during its transport and residence in the air.

Report Part A: Generation and Physical Monitoring of Aerosols

List of Contents.

Part A

Generation and Physical Monitoring of Breathable Aerosols of Polymeric 4,4 - Diphenylmethane - Diisocyanate (MDI)

Author: Dr. A. Bürkholz

1. Description of Objectives

Inhalation experiments on animals require an aerosol of size 0.3 to 3 µm. This size range was established by the competent technical committees of the I.I.I.; it marks the so-called alveolar range of particle deposition. The particle concentrations should be approximately 1 mg/m^3 breathing air for the long-term studies (2 years with 5 days per week) and approximately 300 mg/m^3 breathing air for the short-term studies (one hour).

According to a telex from Dr. D. Clark* dated 15th January 1979, the volume of the inhalation chamber will be 10 m^3 and the volume flow 5 m^3/min. Thus, all aerosol concentrations are to be referred to an airflow of 300 m^3/h.

It was our task to develop and test techniques for generating, measuring and monitoring aerosols of suitable MDI substances, while complying with the data stated above.

(Literature dealing with the definitions and problems of particle inhalation and deposition is cited under (1 , 2 , 3).

2. Test chemicals

In order to avoid possible harm to laboratory personnel all preliminary tests were done without using MDI. So for all atomization tests to determine suitable nozzle units and the necessary atomization

---

*Dr. D. Clark, Shell, is Chairmen of the I.I.I. Ad Hoc Committee to prepare the MDI long term inhalation study.

conditions, an oil as a substitute liquid was used (compressor oil V 100, viscosity at room temperature 300 cP, density 0.89 g/cm^3).

The viscosity vs. temperature of the polymeric MDI tested (Desmodur 44 V 20, Bayer AG) is shown in Fig. 1.

The material has the following specification:

NCO - content	:	30 - 32 %
Total chlorine	:	0.8 % max.
Hydrolysable chlorine	:	0.3 % max.
Sediment	:	1 % max.
Phenylisocyanate	:	0.01 % max.

3. Experimental Set-Up

3.1 Test Rigs and Health Precautions

In view of the dangerous nature of certain aerosols, special measures had to be taken in order to eliminate the possibility of danger to laboratory staff.

The regulations (4) published by the International Isocyanate Institute were observed with respect to general safety precautions.

Since it was impossible to work beneath a hood due to the large dimensions of the equipment, a special open air test rig was set up. The air had to be controlled and atomization had to be accomplished in such a way as to prevent aerosols and spray escaping to the outside. The waste air (300 m^3/h) was discharged above roof level after passing through a filter. The filter selected garantees separation of the major part of the fine aerosols. It would be recommendable to use the same type of filter for subsequent animal experiments. The aerosol generator was located in front of the open end of an approx. 8 m long mixing line of 15 cm diameter. A fan was used to suck ambient air into the pipeline to act as the carrier gas for the aerosols. The sampling points for the aerosol samples and the measuring point for the air speed were located upstream of the filter. The structure is shown in schematic form in Fig. 2.

In order to study the chemical stability of the aerosols, it later proved necessary to pass the aerosol flow through a"residence chamber" simulating the animal exposure chamber to be used in the long term animal study. The chamber consisted of a wooden frame and plastic sheeting, having the dimensions 2 x 2 x 1.7 m^3 = 7 m^3. If the gas throughput is varied approximately, this chamber can be used to achieve residence time equal to or greater than those in the planned chamber of 10 m^3 capacity. The chamber was located at the end of the mixing line. A schematic diagramm of this set-up is given in Fig. 3.

For all atomization tests to determine suitable nozzle units and the necessary atomization conditions, the substitute liquid as described under 2 was used. Test runs with this substitute liquid were done in

the laboratory using a test-rig very similar to the one shown in Figure 2. Later, a static mixer was added to this unit to study the possibilities of feeding the residence chamber with a homogeneous aerosol by eliminating the use of prohibitively long mixing tubes.

3.2 Generators for Liquid Aerosols

3.2.1 Prior Selection of Suitable Generators

Table 2.1 in (5) provides a summary of all the methods of atomizing liquids which are open to consideration. Experience has shown that both spinning disk atomizers and also one-component nozzles (3) yield a droplet spectrum which is too coarse. In principle, ultrasonic atomizers (6) are suitable for producing fine aerosols. However, according to information provided by a manufacturer (7), the ultrasonic atomizers available on the market are restricted to aequeous liquids, since more viscous oils (MDI has a viscosity of approx. 300 cP) absorb the second energy. We were, therefore, of the opinion that two-component nozzles would be most suitable.

Table 3 in (8) provides a summary of commercial two-component nozzles. However, the information provided there is inadequate for selection of the most suitable units, and a systematic test of all units was impossible for cost reasons. Detailed information was found in one company prospectus (9). Subsequently this generator has been ordered and tested on a loan basis. Unfortunately, it did not comply with the requirements imposed. Therefore, the majority of the work had to be concentrated on testing and adapting the nozzle units available in our own laboratory.

It proved impossible to obtain a variation in the aerosol concentration at a ratio of 1 : 300 mg/m^3 on the same unit merely by changing the atomization parameters. Thus, different atomizing nozzles had to be provided for the high concentration and for the low concentration.

3.2.2 Generators for Low Concentrations

Modified medical inhalation nozzles proved to be most suitable for generating aerosol concentrations of about 1 mg/m^3 with droplet sizes 3 µm. Figure 4 shows their structure. Propellant gas is blown through a central pressure line to blow against a bracket. At each side of the bracket there is the end of a suction line through which the liquid is drawn upward. The aerosol emerges sideways from the head piece. The housing and nozzle insert are made of stainless steel in order to exclude the possibility of corrosion.

The amount of fineness of the generated aerosol depend not only on the atomizing properties of the liquid, but also on the propellant pressure and the width of the bores.

3.2.3 Generators for High Concentrations

It proved extremely difficult to generate sprays smaller than 3 µm in concentrations of 300 mg/m^3. A type 970 nozzle made by the Schlick company (10) appeared to be most suitable. When using this nozzle a certain pressure must be built up above the liquid. For this purpose a pressure vessel was made from which the liquid is passed via a hose to the nozzle. The pressure is built up via a gas cylinder. The amount of liquid being atomized can also be influenced by changing the gap width at the nozzle.

The structure is shown in schematic form in Fig. 5. Two nozzles were combined into a single unit; most probably a three-nozzle combination has to be provided for subsequent toxicological studies.

3.3 Separation of Coarse Particles > 3 µm

Every atomizing process produces not only the fine droplets but also more coarse droplets. If an aerosol < 3 µm is required, the coarse portion must be removed.

In principle, it is possible to pass the intire airflow of 300 m^3/h through a suitable separator. The separator should require a minimum of maintenance and should be easy to clean. Furthermore, it should not lead to clog g. Cyclones would appear to be most suitable for this purpose. ver, the pressure drop created in the cyclones would, during s cion operation, cause an excessive vacuum in the inhalation chamber. Thus, it appears better to separate the coarse portion directly in the atomizing glow, i.e. directly downstream of the generator, if at all possible.

3.3.1 Separators for Low Concentrations

We considered it best to use a small cyclone for separating the coarse portion. In an extensive series of measurements, the best lay-out and required operating conditions of the cyclone were determined. Fig. 4 shows the structure in schematic form. The outlet of the nozzle is connected to the tangential inlet tube of the cyclone. A hose emerges in the adapter, through which supply air can be fed in from a nitrogen cylinder. The fine aerosol departs from the cyclone through the axial exit tube and is transported by the carrier air into the mixing line. The droplets separated in the cyclone are collected in a flangemounted vessel which is provided with a drain.

By varying the air supply, the separation characteristics can also be changed, i.e. the fineness of the droplets spectrum at the cyclone outlet.

3.3.2 Separators for High Concentrations

When using the Schlick nozzles, both the propellant air volume and also the amount of coarse spray are considerably higher than for the nozzles for low concentrations. The dimensions of the cyclone must be correspondingly larger. Figure 5 shows its structure in schmeatic form. The two nozzles are accomodated in a tangential inlet pipe of a cyclone. There is a connection for the

supply air on the exit tube. The supply air ensures a slight vacuum in the cyclone, sucking a little ambient air alongside the nozzles so that no spray can escape to the outside. This ambient air and atomizing air together transport the fine spray via the exit tube to the mixing line, whereas the coarse spray runs down through the cyclone. The amount of coarse spray is relatively high at this stage, but the cyclone is capable of retaining this quantity.

4. Measuring and Monitoring the Aerosol

The generation of an aerosol having a specified concentration and particle size distribution required a great number of aerosol measurements, most of which were accomplished by means of cascade impactors. Light scattering instruments were also used in parallel, these having been hired from the manufacturers.

4.1 Cascade Impactor +)

In this process, a vacuum pump sucks a measuring gas flow of approx. 5 l/min via a sampling probe and through a cascade impactor. The sampling time is determined by the aerosol concentration, generally being from several minutes up to 2 hours. The amount of gas sampled is monitored by a gas meter.

In the cascade impactor, the aerosol droplets are separated by size, being deposited on small glass plates. The leaflet attached to this report includes an illustration of the unit and a schematic drawing of the separation process. In more detail this impactor is described in (15). The mean droplet sizes of the fractions are known from calibration measurements. The amounts deposited must not be more than a few milligrams, the weight being determined by weighing on a sensitive balance. The deposit weight and sampling volume are used to calculate the aerosol concentration in mg/m^3.

+) See leaflet in appendix.

The advantage of the cascade impactor over other, counting measuring equipment, is that direct masses and not particle counts are measured. Limitations of maximum concentrations of aerosol or dust particles which are set for occupational hygiene reasons and for environmental are referring to masses and not counts of particles. In addition, separation is accomplished in accordance with the aerodynamic particle diameter, as is primarily the case in the lungs.

Since the aerosol particles are collected in the cascade impactor, they can subsequently be further examined. The amounts collected are only in the range of a few milligrams, but are generally adequate for sensitive analytical studies.

4.2 Light Scattering Instruments

During long-term experiments with aerosol concentrations of 1 mg/m^3, sampling time of approx. 2 hours are required in order to obtain weighable amounts in the impactor. Therefore, it would be recommendable to use a monitor with instantaneous indication for monitoring in the aerosol flow. In principle, scattered light measuring equipment is suitable for this purpose. However, at a level of 1 mg/m^3 and particles between 0.3 and 3 μm, such equipment is already working at the upper limit of its counting capacity.

It came out from discussions with four manufacturers (11, 12, 13, 14) that they were unable to provide any binding garantees as to the suitability of this equipment. Therefore, it was necessary to carry out tests under the corresponding experimental conditions. The equipment of companies (13) and (14), was made available for a rental fee.

Light scattering instruments are planned for the long-term experiments, in order to be able to continuously monitor the constant fineness and concentration of the aerosol. It should, therefore, permit immediate indication in the event that any nozzle should become clogged. The instruments draws in test gas from the measuring

line via a probe element, transporting the gas into a measuring cell. The measuring cell is illuminated by a sharply focused light beam. Each individual particle struck by the light beam in turn scatters light which is then collected and analyzed. The intensity of the scattered light pulse is dependent on particle size. The instrument prints out the results in the form of numbers of particles contained in a certain prescribed measured volume and lying within certain size ranges.

The following three equipment types were tested:

Manufacturer	Type	Price (approx.) DM	Size ranges
Kontron	200-6	20.000,--	0,5 - 1 - 2 - 5 - 10 µm
Royco	225	30.000,--	0,3 - 0,5 - 0,7 - 1,4 - 3 µm
Royco	226	40.000,--	0,1 to 6,1 µm (16classes)

The Kontron 200-6 and Royco 225 each have 5 measuring ranges for particle size, some of which ca be varied. The Royco 226 is a laser unit on which the particles are classified into 16 preset size classes. All of the units have their own suction pump and are provided with printers.

A calibration curve for the Royco 225 counter is given in Fig. 6.

5. Performance of the Atomizing Experiments

5.1 Atomizing Experiments with the Substitute Liquid

5.1.1 Low Concentrations

5.1.1.1 Measurements with Cascade Impactor

A large number of atomizing experiments was required in order to find and test suitable generator layouts. Each atomizing experiment was accompanied by aerosol analysis with the cascade impactor.

The problem involved with low concentrations was that of obtaining an adequately diluted aerosol of the required fineness. For this purpose, the bores in both the suction lines and also the pressure lines of the spraying nozzle were varied in the range from 0.5 to 2 mm. The propellant gas pressure was adjusted between 0.5 and 10 bar. In addition, the air supply at the cyclone separator was also changed. Figure 7 shows a number of size distributions of a nozzle having 1 mm bores; these comply with the requirements both with respect to the amount (300 m^3/h) and also the fineness of the aerosols. The curve gives the mass percentages of the droplets above reference droplet size.

5.1.1.2 Measurements with Light Scattering Instruments

5.1.1.2.1 Relationship Between Particle Counts and Aerosol Concentrations

Light scattering instruments have different maximum counting rates. In order to test the reliability of the indication at 1mg/m^3, the particle counts were measured as a function of aerosol concentrations and compared to the impactor values.

For this purpose the atomizing nozzle was set to an aerosol concentration (substitute liquid) of approx. 1 mg/m^3 in an airflow of 300 m^3/h. Under constant atomizing conditions, the airflow was then gradually reduced to 200, 100 and 50 m^3/h, meaning that aerosol concentrations of 1.5, 3 and 6 mg/m^3 were correspondingly generated. The measured particle counts have been compiled in Table 1 in units of 10^3. If the measured values are referred to the set values obtained by extrapolating the particle counts for 300 m^3/h, the corresponding percentage figures are obtained. The particle counts

refer to 280 ml for the Kontron and Royco 225 units, and to 1000 ml for the Royco 226 unit. Practically no particles greater than 3 µm were measured.

Where "o.r." is stated for the Kontron unit, this means over range, i.e. an excessively high counting rate. This occurs in the > 0.5 µm channel even at 300 m^3/h, the higher channels also becoming involved at 50 m^3/h. The Kontron unit is therefore unsuitable for use as a Monitor.

On the other hand, the two Royco units indicate particle counts in the range 0.3 to 3 µm which are roughly proportional to the aerosol concentrations. Surprisingly, the particle counts below 0.4 µm do not increase with increasing aerosol concentration, but decrease instead. Thus, a higher aerosol concentration and a longer residence time in the mixing line have the effect of increasing the degree of agglomeration of the smaller particles. At the same time, the proportion of larger particles increases disproportionately rapidly due to absorption of the smaller particles.

The particle counts and sizes can be used to calculate the aerosol concentrations. In Table 2, the values of the Royco 225 are compared to the value obtained from impactor measurements taken at the same time. The concentrations determined by light scattering measurements are 20 - 40 % below the impactor concentrations.

Probably the main reason for this is the difficulty involved in determining mass distributions on the basis of count distributions. Furthermore, according to Fig. 6, the Royco 225 unit has a range between 0.7 and 1.4 µm where there is no clear relationship between measuring signal and particle size.

In Figs. 8 and 9, size distributions of aerosols measured with the light scattering instruments are compared with results of the cascade impactor. Curves are again cumulative weight % oversize.

There is a fairly good agreement in size distribution between the different methods. However, when counting data are used to calculate aerosol concentrations, these values account for only about 30 % of the values obtained by weighing the impactor deposits. Although there are several approaches to explain this difference a definite interpretation is not available to date. Certainly the problem must be sought on the light scattering instrument. This that calibration is needed in case the light scattering instrument is used for monitoring the aerosol concentration in the inhalation chamber.

5.1.1.2.2 Static Mixer for the Aerosol Flow and the Carrier Air

When entering the inhalation cage, the aerosol flow must have been mixed completely with the carrier air flow, because the test animals would otherwise be exposed to varying concentrations. In our experiments mixing was ensured by using a pipeline of several metres length; during the inhalation tests to be implemented at a later stage, it is possible that this pipeline may not be applicable for reasons of space. In this case, it will be necessary to use a static mixer. We tested a mixer manufactured by the Sulzer Company of Winterthur (Melapack). For this purpose, the aerosol distribution was measured over the pipe cross-section at a distance of 1.6 m from the aerosol generator, measurements being accomplished both with and without the 0.34 m long mixer.

Figure 10 shows the particle counts (referred to 280 ml, as in Figs. 11 and 13) measured with a Royco 225 unit as a function of the distance from the pipe wall. The diameter of the pipe is 200 mm. The abscissa is a time axis, there being approx. 1 min between each of the measuring points.

If no mixer is used, the particle counts shows considerable temporary variations, particularly at the pipe walls. On the other hand, the particle counts are remarkably constant and equally distributed if a mixer is used.

5.1.1.2.3 Effect of Pressure on Atomization

The great effect of the propellant pressure on atomization was already established during previous experiments with the cascade impactor. For example, without using a cyclone, 3.8, 18 and 12 mg/m^3 were measured with the impactor at pressures of 2, 5 and 7 bar. The particle counts measured in the Royco 225 counter for step-by-step pressure increases have been entered in Fig. 11. Again, a drop is noted at 7 bar. Nevertheless, by changing the atomization pressure, it is possible to vary the aerosol concentration by at least one power of ten.

5.1.2 High Concentrations

Numerous experiments also had to be carried out with the Schlick nozzles in order to determine the optimum atomization conditions. It is possible, for example, to change the gap width of the nozzles, propellant gas pressure and material pressure being varied within the range of up to 10 bar. The dimensions of the downstream cyclons and the supply air volume also had to be varied. By combining two Schlick nozzles with a maximum gap width and using the atomization parameters stated in Fig. 12, it was again possible to generate a suitable aerosol.

5.2 Atomizing Experiments with MDI

Having determined the optimum atomization and separation conditions after a lenghty experimental stage, experiments with MDI were started.

5.2.1 Low Concentrations

Monitoring of MDI-Aerosols of low concentrations was done with cascade impactors and light-scattering instruments, often using both devices in parallel.

When atomizing MDI on the open-air site, the temperature variations due to the influence of weather conditions had to be taken into account.

It was taken care that the temperature of the MDI in the nozzle was subsequently measured by means of a thermocouple. It was observed in one case that during approx. 1 hour the temperature dropped from 13°C to 8°C and the concentration fell to roughly half the original level. It is obvious that the reason for this change is the increasing viscosity of the MDI.

The effect of temperature on the aerosol concentration is shown in Fig. 13. To obtain this data the MDI was slowly heated during atomization from 10°C to 40°C. The particle increase lies between 1 and 2 powers of 10. For the inhalation study it is important that depending on the temperature of the test room the aerosol generator has to be kept at a constant temperature. When the temperature is constant, a constant size spectrum over time is also obtained.

Thus, the temperature of the aerosol generator on our open-air measuring facility was kept constant by means of strip heaters, thermocouple and temperature controller. It may be recommendable to use a Thermostat for the long term study.

The filling volume of the nozzle should be adequate for 4 - 6 hours of operation. Clogging of the bores did not occur. However, since MDI can react with moisture of the air, the nozzle must be carefully washed out with acetone and cleaned carefully after each cycle. Cylinder nitrogen should be used as the propellant for the same reason.

Fig. 14 shows size distribution curves measured with the cascade impactor. Atomization data and concentrations are also noted.

In Fig. 15 the distribution curves of the Royco 226 unit are compared with those of the impactor. The light scattering curve is shifted into the fine range, the concentrations being approximately only 10 % of the values measured in the impactor. During an inspection of the unit by the supplier, it was found that the unit was no longer correctly focused. If the distribution curve is corrected to that of the cascade impactor, concentrations amounting to approx. 30 % of the impactor values are obtained. As already mentioned before the exact cause of

this difference is not known.

The course of the distribution curves also shows that the particle sizes are almost completely restricted to the range from 0.3 to 3 µm, i.e. that they also have a bottom limit.

The above mentioned deviations have no influence on the suitability of light scattering equipment as monitoring systems. In principle, both of the Royco units are suitable for this purpose. However, our experience showed that the 225 appeared to be more sturdy. In the search for possible sources of error, the weighing equipment was also checked. Thus, for example, comparison measurements were made using an equivalent balance in a different laboratory department. Furthermore, NaCl aerosols were generated and collected in the impactor. The NaCl deposits were studied both gravimetrically and analytically. All of these studies confirmed the reliability of the impactor method and of gravimetry.

However, it must be kept in mind that sampling of very low concentrations with the cascade impactor and subsequent weighing of the deposits requires careful handling. Since the sampling flow is set to 0.3 m^3/h, it needs a sampling time of more than 3 hours to collect the amount of 1 mg out of an aerosol of 1 mg/m^3. This amount of 1 mg is again subdivided in up to 10 deposits on the 10 impaction stages. The precision of the weighing process must be fairly better than 0.1 mg. In addition, the MDI-deposits adhere firmly to the glass plates and must be washed off very carefully.

When measuring very low aerosol concentrations, the result can be further falsified by the collection of dust whose presence in the ambient air cannot be fully excluded. So, when performing aerosol sampling with the cascade impactor for analytical studies (as described in Part B), the amount of dust in the air had to be determined by a second cascade impactor. This sampling was done either outside the test or at the entry of it. Dust concentrations measured at six different days ranged from 0.16 mg/m^3 up to 1.6 mg/m^3.

Measuring dust concentrations with cascade impactors is very tedious and can be done much more easily by light scattering devices.

5.2.2 Intermediate Concentrations.

Sampling at Entry and Exit of Residence Chamber.

In connection with the analytical studies described in Part B, it was desirable to work with higher concentrations than 1 mg/m^3. This ca be done by two different approaches: one can reduce the air flow in the test tube or one can adapt the aerosol generator to higher yields. Both measures were taken, so that aerosol concentrations could be produced ranging from 1 to 60 mg/m^3. In the test rig used to date, the aerosols were only exposed to ambient air for a few seconds prior to being collected in the measuring device. However, the mean residence time in the inhalation chamber planned for later use is 2 mins. It was for this reason that the test rig was connected to the residence chamber; as described in 3.1. during the associated experiment, the aerosol samples were taken upstream and downstream of the chamber. The results of the experiments have been compiled in Table 3.

The 2nd column states the air volumes sucked through the cabin. These yield the mean residence times of the aerosol stated in the 4th column. The figures in the 3rd column are sampling times. All sampling times are greater than the residence times.

Columns 5 and 6 show the absolute amounts of MDI sampled before and behind the residence chamber as determined by weighing the impactor plates. Columns 7 and 8 give concentrations of the aerosol when entering and leaving the chamber, calculated from the value of columns 5 and 6. Both concentrations correspond fairly well, the differences being mainly due to experimental scatter. So there seems to be no noticeable loss of aerosol in the chamber. Results of analytical measurements will be described in part B.

5.2.3 High Concentrations

When producing high concentrations of MDI aerosol, the Schlick nozzles were sometimes blocked after a short time. Clogging of the nozzles due to solid impurities in the MDI on the formation of solid reaction products was obviously the reason.

In order to remedy this situation, filters were installed in the feed line from the supply tank to the nozzles. Furthermore, the MDI was warmed and filtered prior to being filled into the supply tank.

The large propellant gas throughput in the Schlick nozzles also caused a noticeable temperature drop which increased the viscosity, thus reducing the atomization rate. It was for this reason that the supply tank was heated.

Figure 16 shows an aerosol size distribution measured with the cascade impactor which complies with the fineness requirements. The amount atomized or the concentration is highly dependent on the temperature of the MDI. If atomization is to be accomplished at room temperature, a third nozzle must also be used in order to attain 300 mg/m^3.

Having taken the above measures, it was possible to atomize the entire contents of the supply tank without the occurrence of clogging. However, with a supply tank capacity of 1.2 l, this took approximately 10 minutes. A correspondingly larger tank will have to be provided for future work.

6. Conclusions

The investigations described in this part of the report have shown the possibility to generate and monitor an aerosol of MDI in concentrations of ca. 1 mg/m^3 and ca. 300 mg/m^3 and with a size distribution ranging from 0.3 to 3 μm. By varying the atomization parameters it is also possible to generate aerosols of intermediate concentrations.

Before planning the final set-up for the inhalation experiments, the test capacities and the test equipment of the institution to run the tests must be known. There are some more points, e.g. deionisation of aerosols which should be discussed. Some of the equipment can be bought on the market (e.g. cascade impactors, light scattering instruments).

The design of the equipment to be constructed for the toxicological study, the technical assistance to be made available during the planning and construction phase and during the performance of the first runs in the laboratory of the toxicology contractor should be subject of a new contract.

Literature

/1/ Jahresversammlung der Gesellschaft für Aerosol-Forschung, Oktober 1979

/2/ J.P. Schreider, J.O. Hutchens
Particle deposition in the guinea pig respiratory tract
J. Aerosol Sci. 10 (1979) S. 399/607

/3/ A. Bürkholz et al
Primäre Tropfengrößenverteilung und atembarer Feinanteil beim Lackspritzen durch Druckluftzerstäuberdüsen
Farbe und Lack 82 (1976) 8, S. 693/698

/4/ International Isocyanate Institute: Technical Information
Recommendations for the Handling of Aromatic Isocyanates
New York, 1976

/5/ VDI-Richtlinie, VDI 3491, Blatt 2
Messen von Partikeln, Herstellungsverfahren für Prüfaerosole; Grundlagen und Übersicht, 1977

/6/ U. Reimann, R. Pohlmann
Optimierung und Vernebelung von Flüssigkeiten mit Ultraschall unter Berücksichtigung der Probleme bei höheren Frequenzen
Forsch.Ing.-Wes. 42 (1976) 1, S. 1/7

/7/ Carl Heyer GmbH, Bad Ems

/8/ VDI-Richtlinie VDI 3491, Blatt 3
Messen von Partikeln, Herstellen von Latex-Aerosolen unter Verwendung von Zerstäuberdüsen, 1979

/9/ Opto-Elektronische Instrumente GmbH, Karlsruhe

/10/ Firma Schlick, 8630 Coburg

/11/ Firma Kratel, 7016 Gerlingen ? - Stuttgart

/12/ Firma Polytec, 7517 Waldbronn-Karlsruhe

/13/ Firma Kontron-Technik, 8057 Eching

/14/ Firma Royco-Instruments, 7250 Leonberg 2

/15/ A. Bürkholz
Eichuntersuchungen an einem Kaskadenimpaktor
Staub - Reinhaltung Luft 33 (1973) 10, S. 397/401

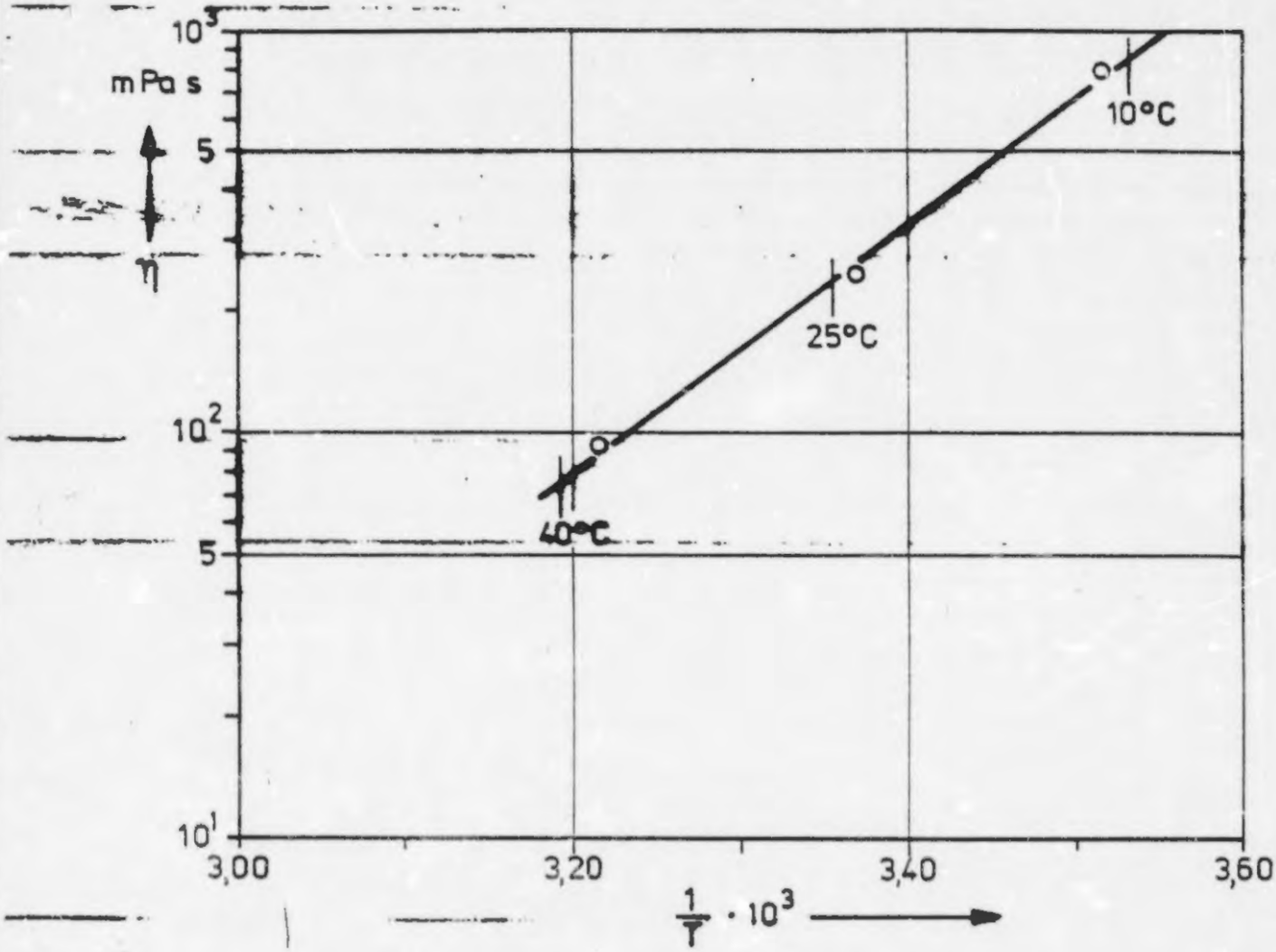


Bild 1: Temperaturabhängigkeit der Viskosität von Isocyanat MDI

Dependence of the viscosity of MDI on temperature.

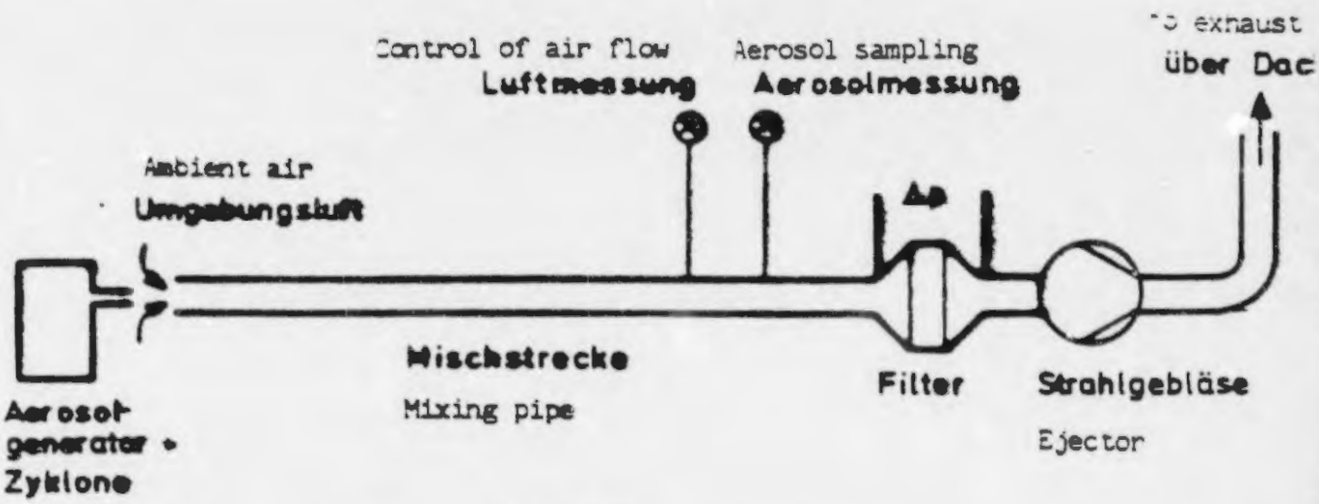


Bild 2: Test rig
Meßstand

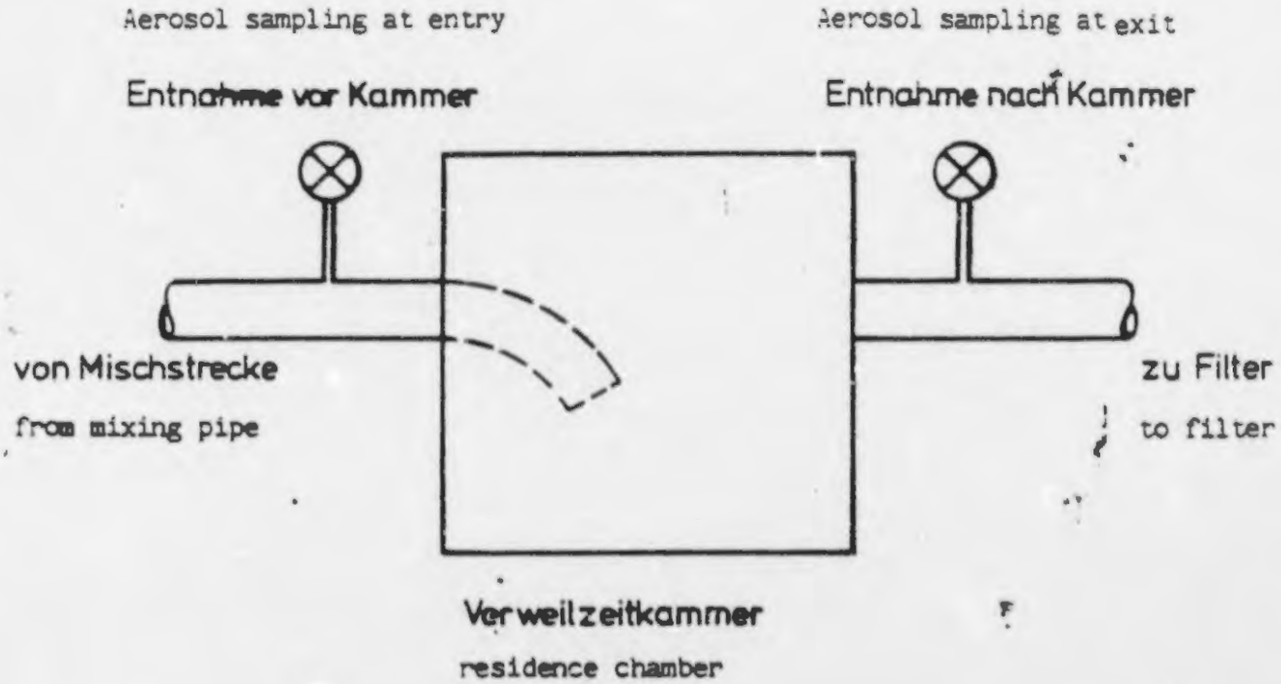


Bild 3: Meßstand mit Verweilzeitkammer

Test rig combined with residence chamber

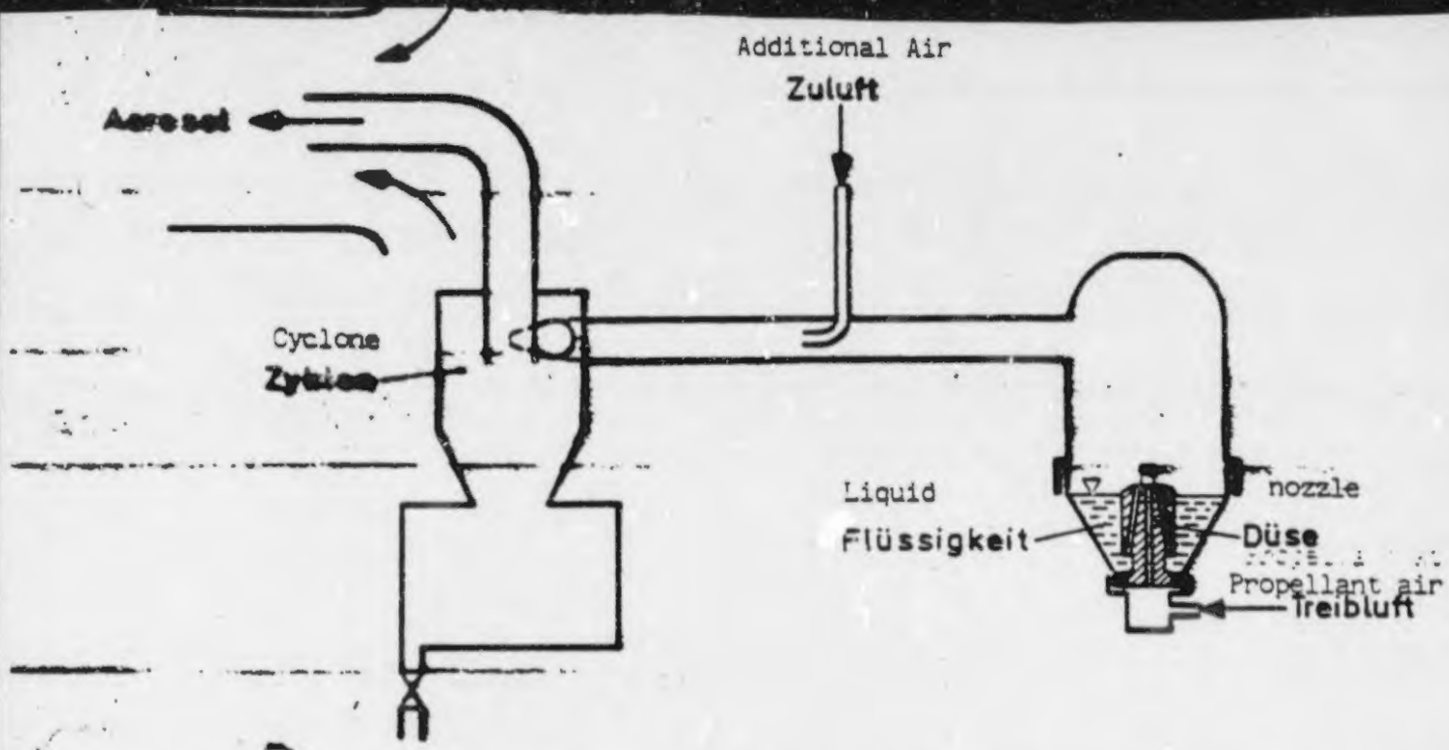


Bild 4: Generator und Abscheider 1 mg/m³, schematisch

Generator and separator, low and intermediate concentrations, schematic

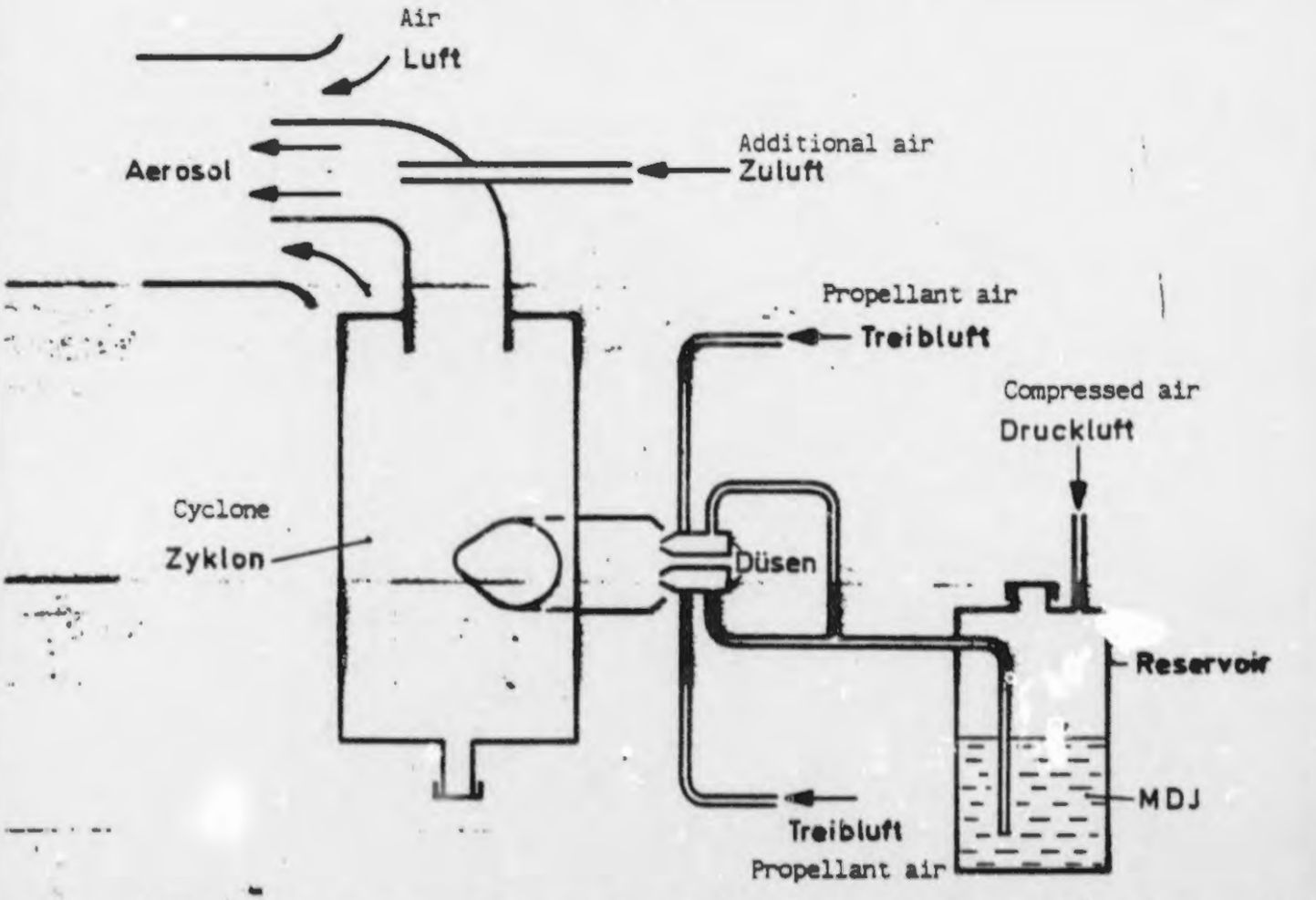


Bild 5: Generator und Abscheider 300 mg/m³, schematisch

Generator and separator, high concentration, schematic

CALIBRATION CURVE FOR

ROYCO PARTICLE COUNTER

DATE: 9-5-79

TECH: TONY B

MODEL 225 S/N 44

SENSOR 241 S/N 441

PLUG-IN 518 S/N 221

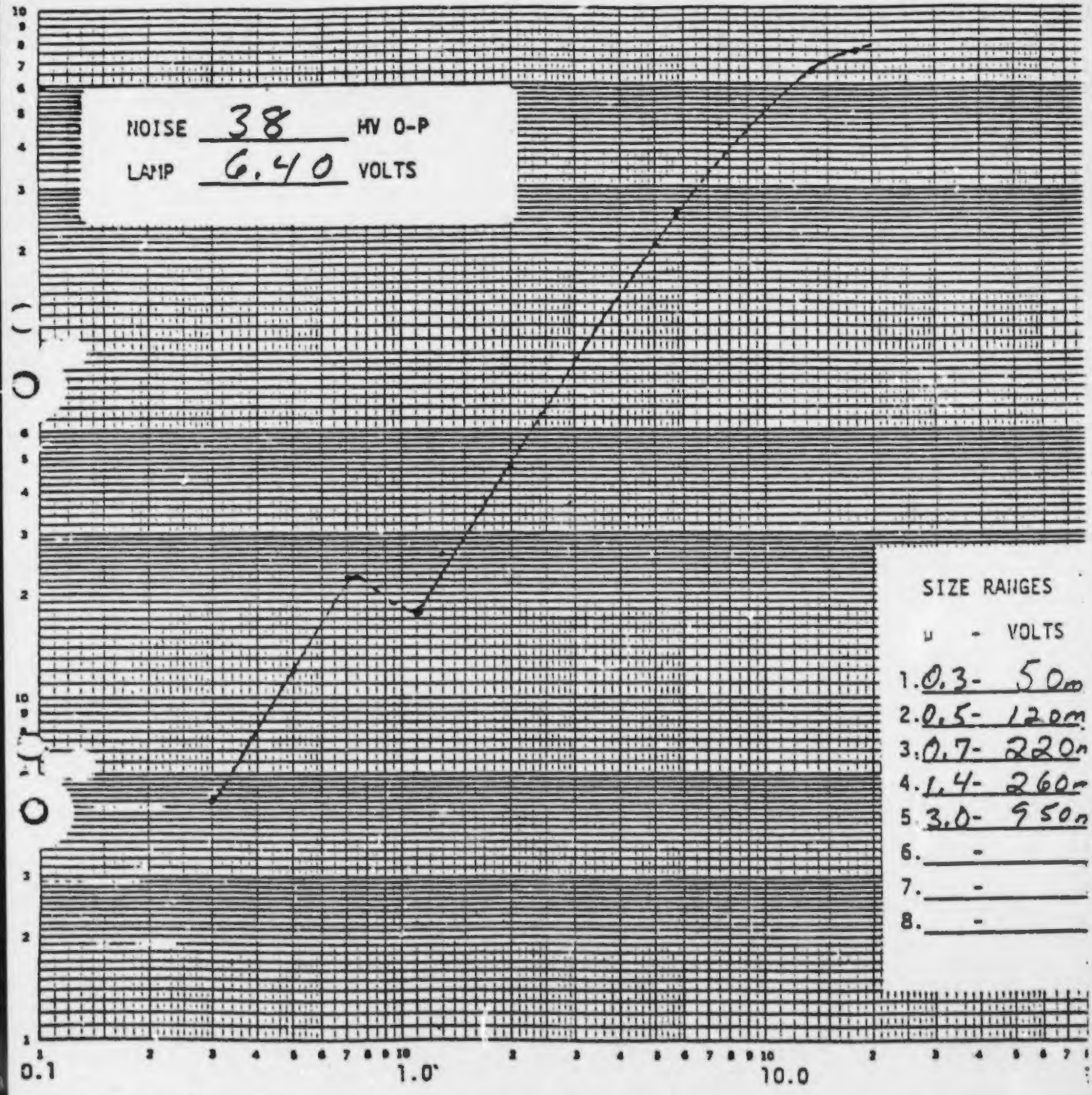
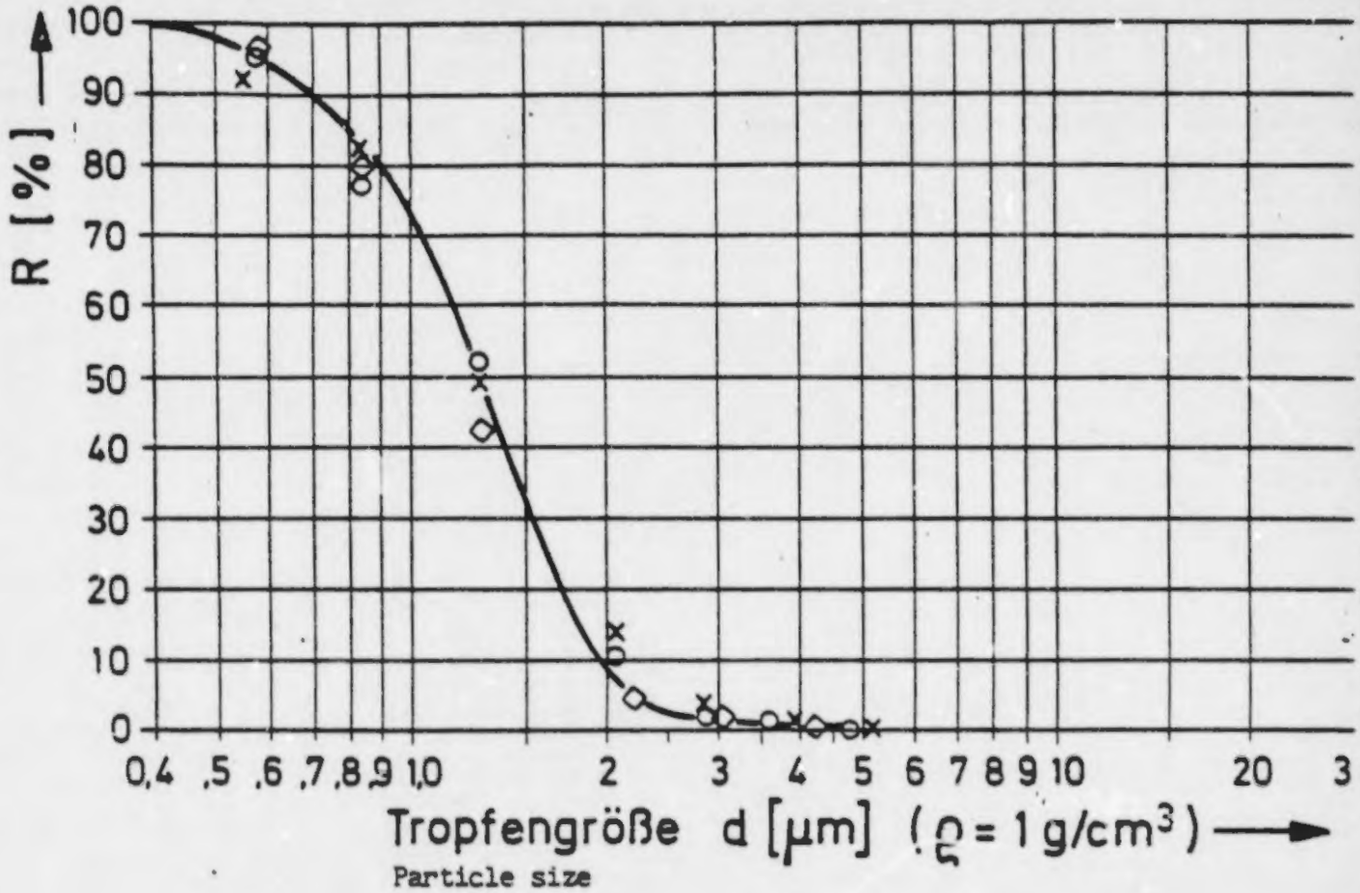


Fig. 6

1/78



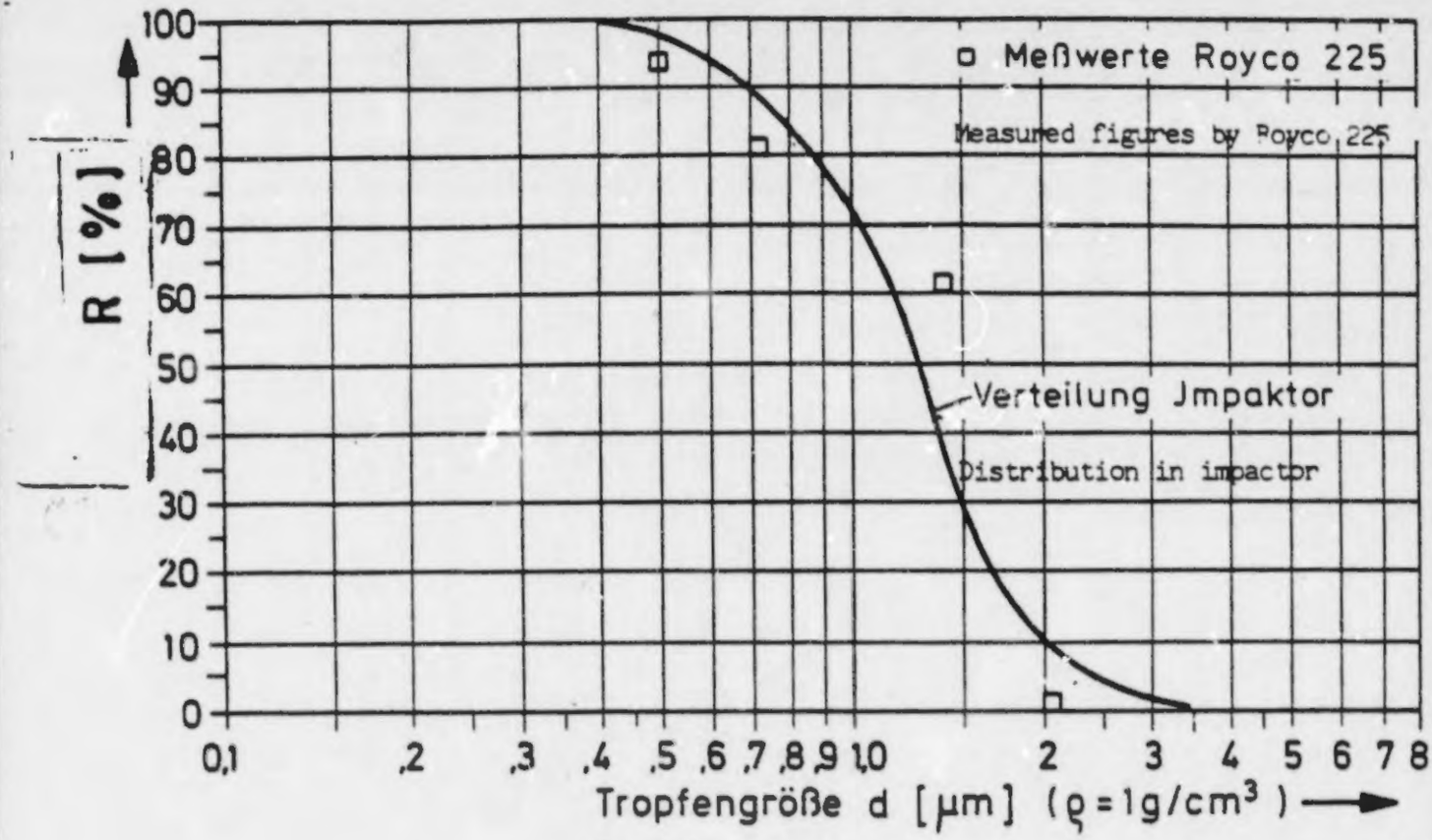
	Propellant air Treibluft bar	Additional air Zuluft bar	Aerosol mg / m³
◇	4	0,6	3,5
○	3	0,6	1,6
×	2	1,2	1,0

Aerosol distributions, substitute liquid.

Bild 7 : Aerosolverteilungen Ersatzflüssigkeit.

Abgewandelte Jnhalationsdüse mit Zyklon

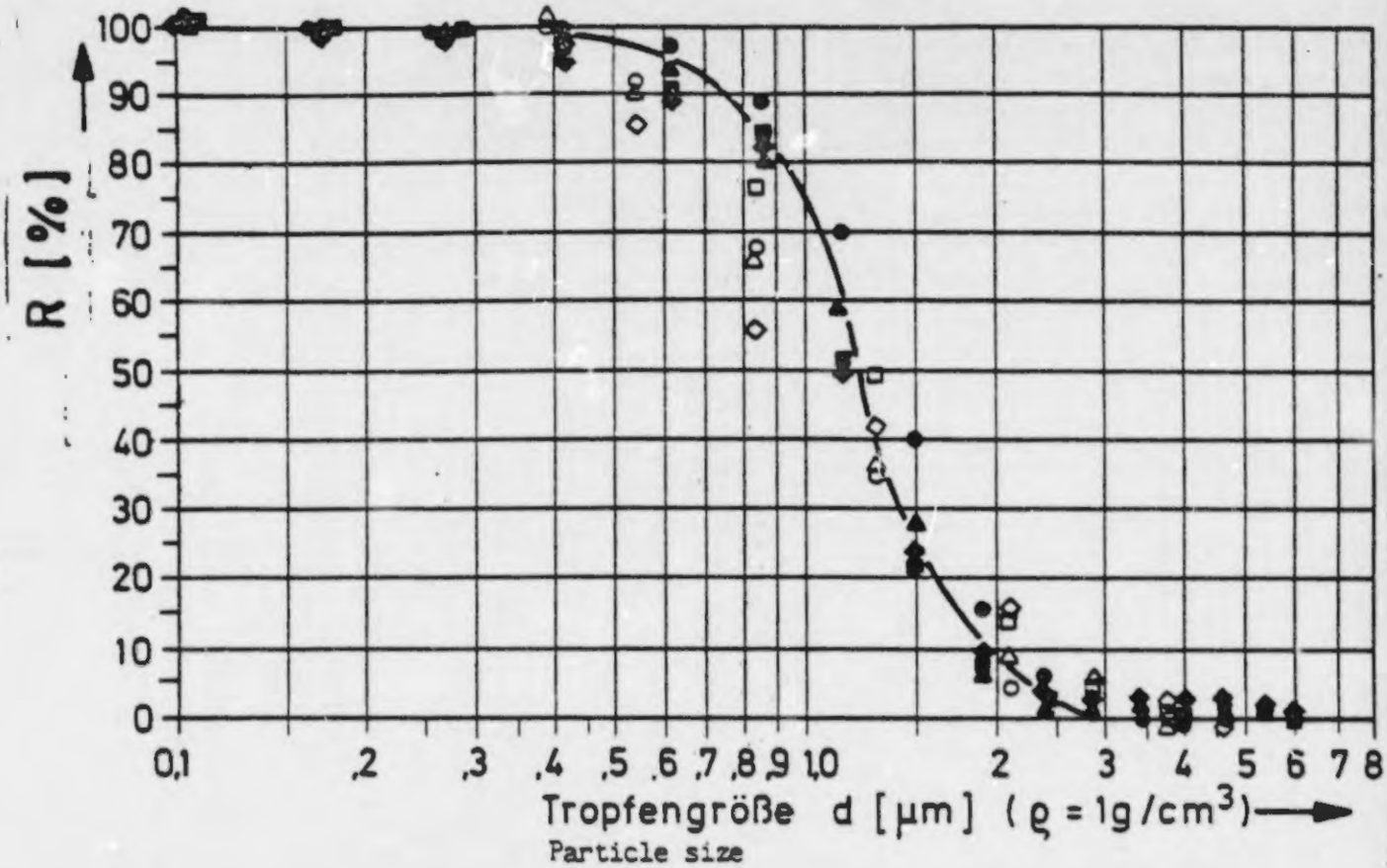
R = Aerosol weight percentage made up by particles > d



Comparison of aerosol size distribution according to cascade impactor and Royco 225 light scattering instrument - Substitute liquid.

Bild 8: Vergleich der Aerosolgrößenverteilung gemäß Kaskadenimpaktor und Streulichtgerät Royco 225 - Ersatzflüssigkeit

R = Aerosol weight percentage made up by particles > d



Symbol	Air flow Durchsatz m^3/h	Aerosol concentration Konzentration mg/m^3	Measuring device Meßgerät
○	50	6,0	Cascade impactor Kaskadenimpaktor
△	100	2,5	
□	200	2,0	
◇	300	1,0	
●	50	1,75	Royco LAS-226
▲	100	0,75	
■	200	0,30	
◆	300	0,27	

Comparison of aerosol size distribution according to cascade impactor and Royco 226 - Substitute liquid.

Bild 9 : Vergleich der Aerosolgrößenverteilung der Ersatzflüssigkeit gemäß Kaskadenimpaktor und Streulichtgerät Royco LAS 226

R - Aerosol weight percentage made up by particles > d

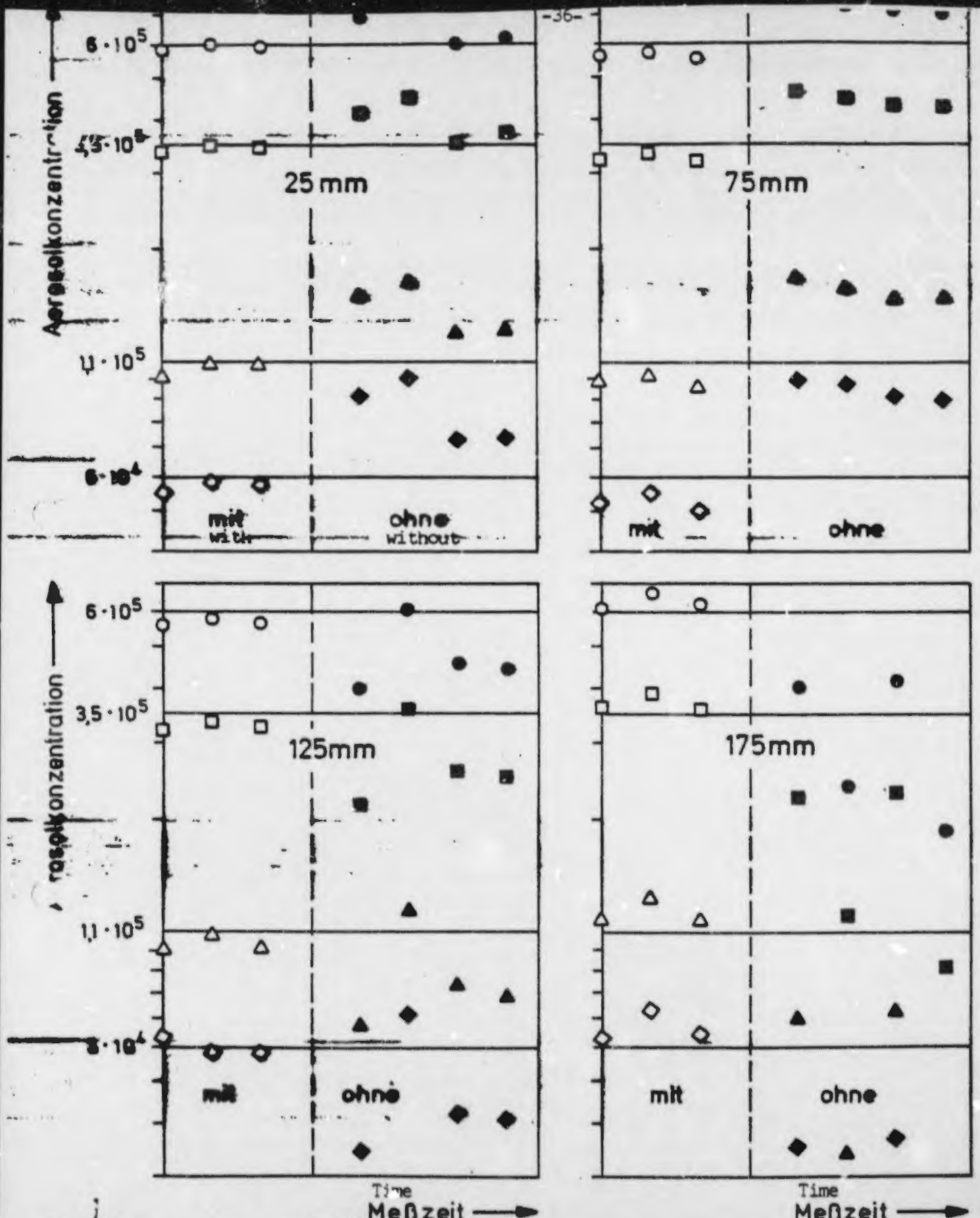
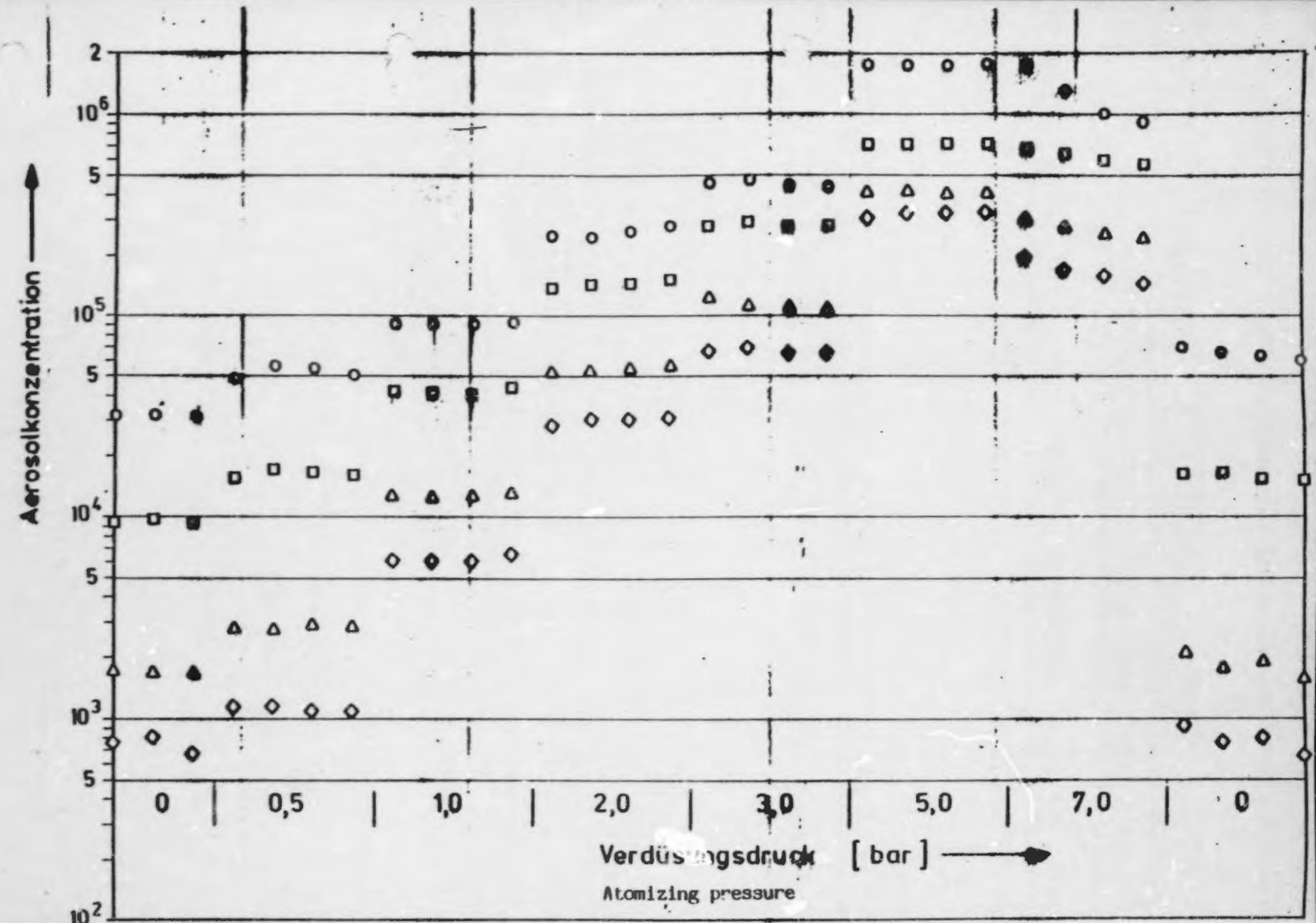


Bild 10: Effect of a static mixer on the aerosol distribution in a pipe of 200 mm diameter over space and time.

Wirkung eines statischen Mischers auf die räumliche und zeitliche Aerosolverteilung in einem Rohrdurchmesser (200 mm).

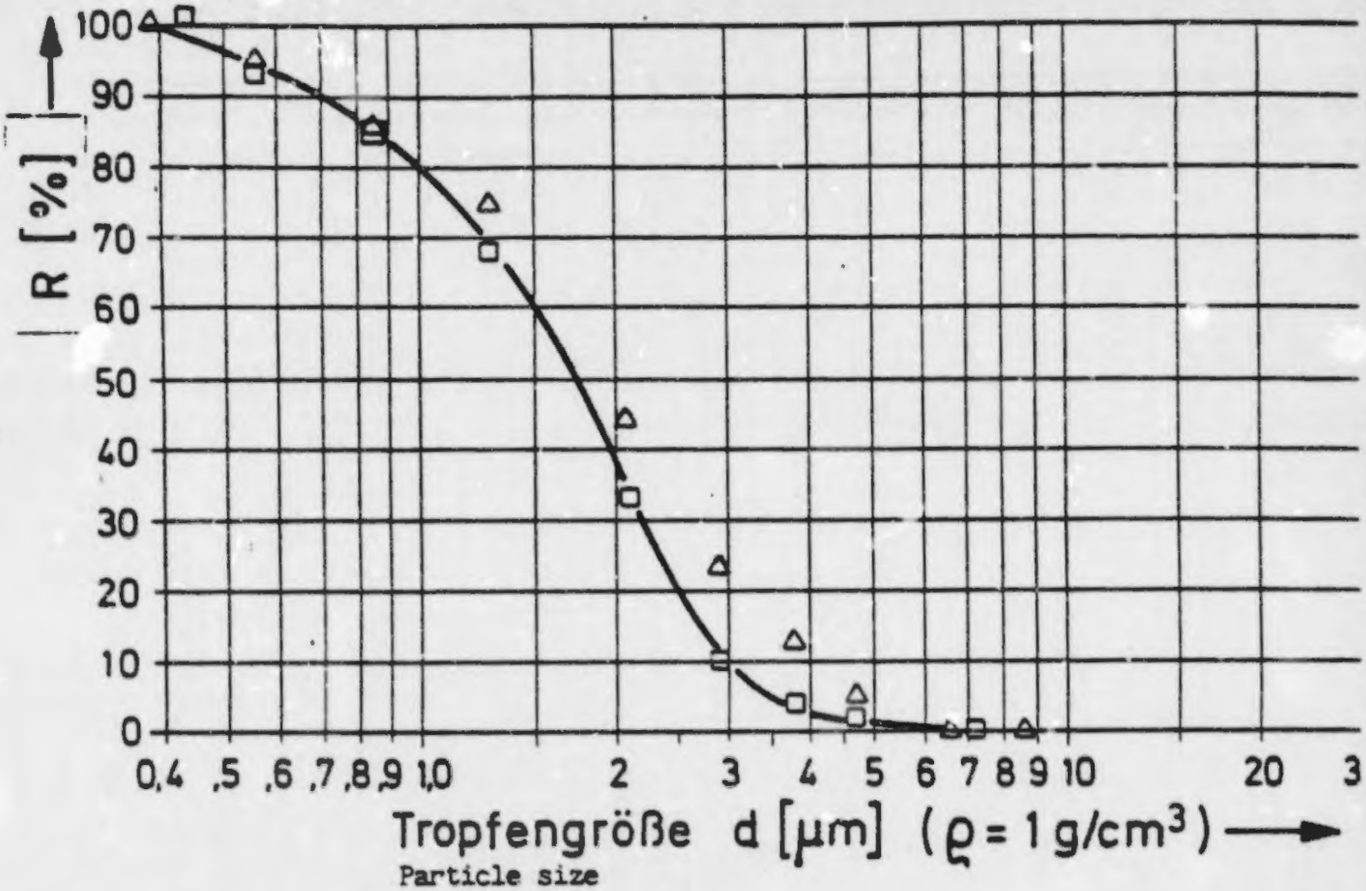
●○ ≙ 0,3 µm ■□ ≙ 0,5 µm ▲△ ≙ 0,7 µm ◆◇ ≙ 1,4 µm



Dependence of the aerosol concentration (substitute liquid) on the atomizing pressure.

Bild 11: Abhängigkeit der Aerosolkonzentration (Ersatzflüssigkeit) vom Verdüsungsdruck

o ≧ 0,3 µm ; □ ≧ 0,5 µm ; △ ≧ 0,7 µm ; ◇ ≧ 1,4 µm



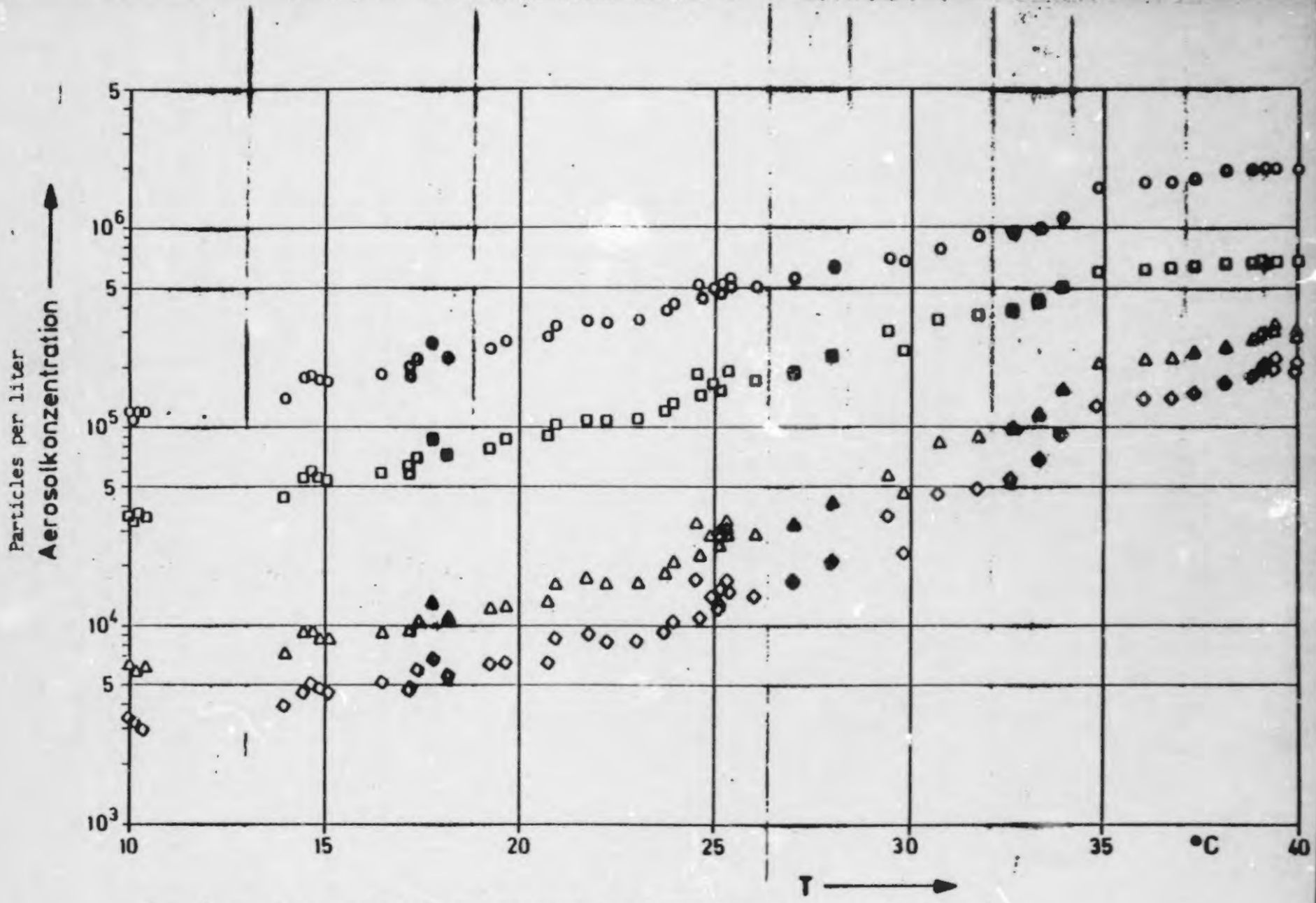
	Propellant air Treibluft bar	Pressure of Additional air Zuluft bar	liquid Material bar	Concentration of Aerosol Aerosol mg/m³
△	10	0,5	8	288
□	10	1,2	10	296

Bild 12: Aerosolverteilungen Ersatzflüssigkeit.

2 Schlick-Düsen mit Zyklon

Aerosol distributions, substitute liquid. 2 Schlick nozzles with cyclone.

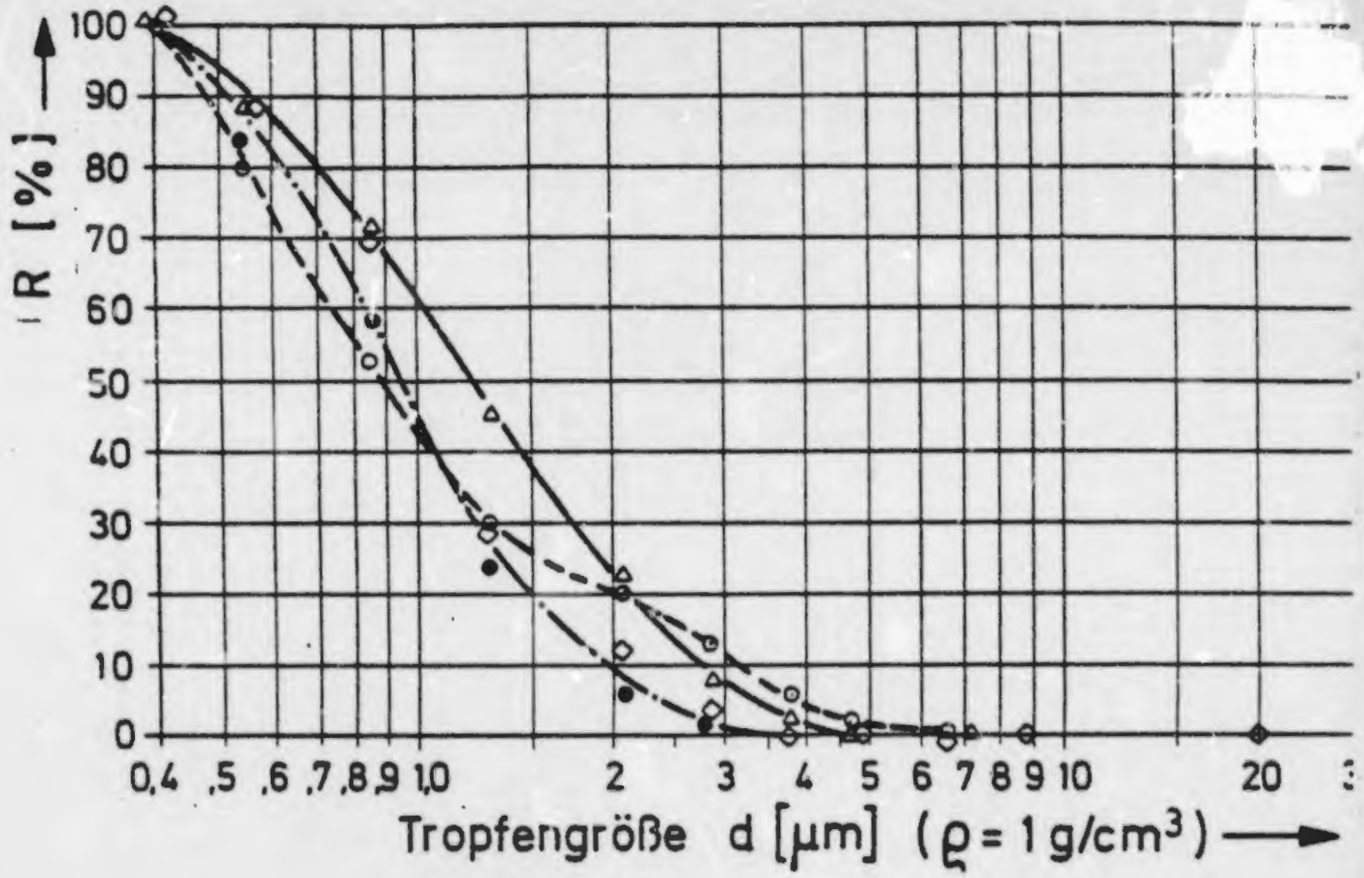
R = Aerosol weight percentage made up by particles> d



Dependence of the aerosol concentration on the temperature of the atomized MDI.

B 1 13: Abhängigkeit der Aerosolkonzentration von der Temperatur des verdüsten MDI

○ ≥ 0.3 µm. □ ≥ 0.5 µm. △ ≥ 0.7 µm; ◇ ≥ 1.4 µm



Particle size

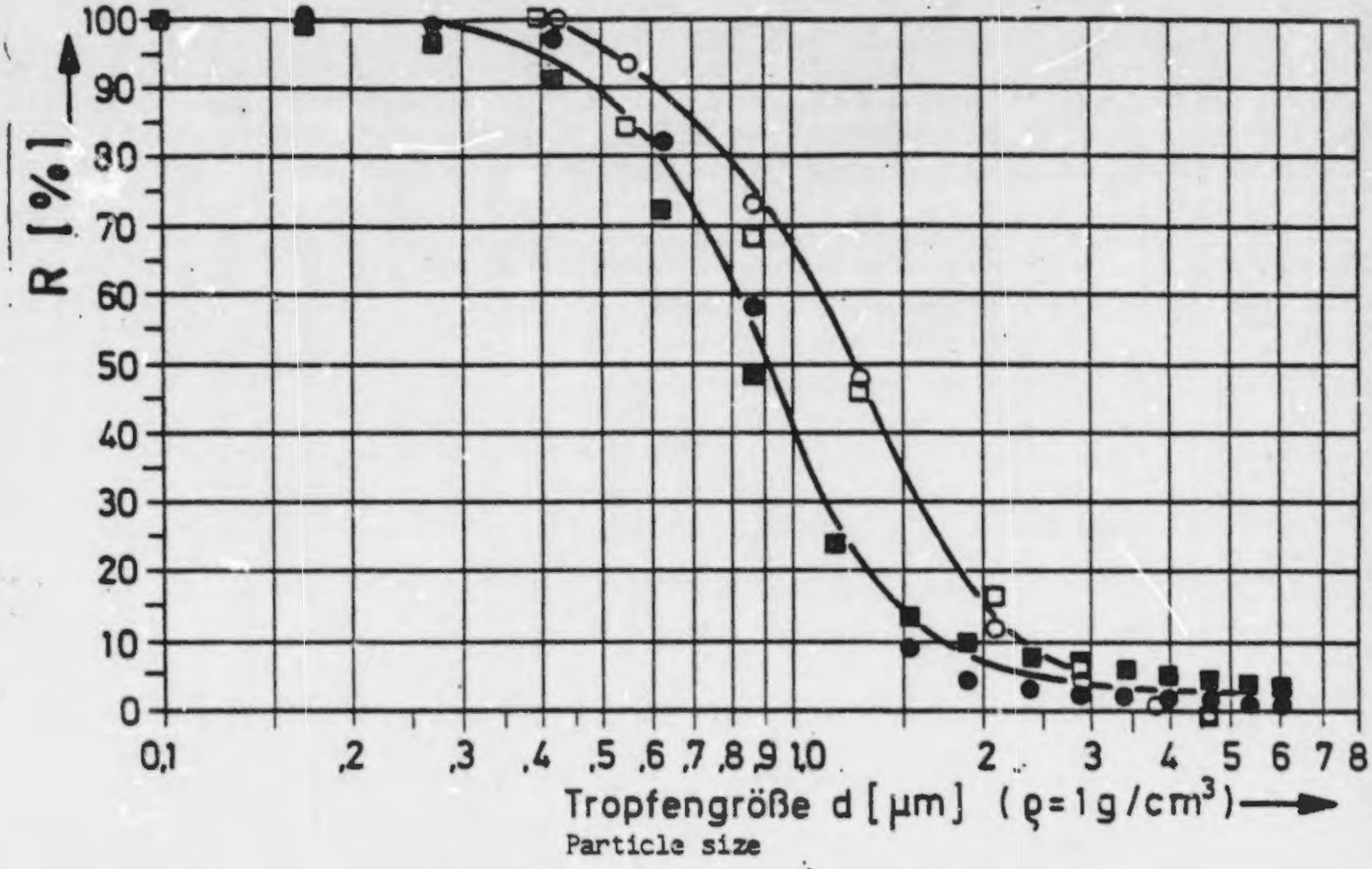
	Propellant air Treibluft bar	Pressure of Additional air Zuluft bar	Concentration of Aerosol mg/m³
◇	6	1,2	2,2
●	4	1,2	1,3
○	2	—	1,3
△	3	—	1,3

R = Aerosol weight percentage made up by particles > d

Bild 44: MDJ - Aerosolverteilungen

Abgewandelte Jnhalationsdüse mit Zyklon

MDI aerosol distributions. Modified inhalation nozzle with cyclone. Low concentrations.

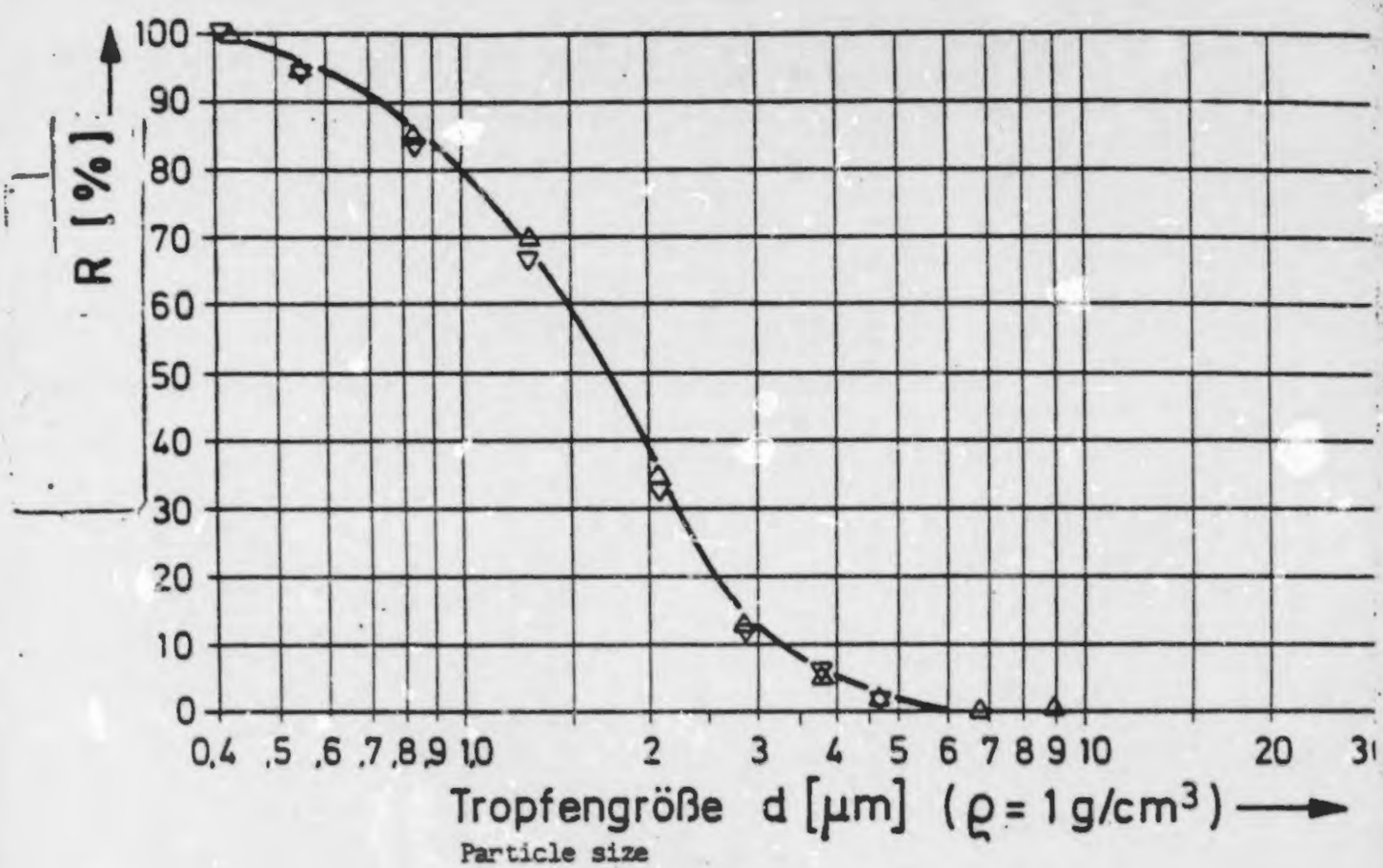


Symbol	Durchsatz m^3/h (Air flow)	Konzentration mg/m^3 (Concentration)	Meßgerät (Measuring device)
○	100	3,75	Cascade impactor Kaskadenimpaktor
□	300	1,19	
●	100	0,37	Royco LAS-226
■	300	0,08	

Bild 15: Vergleich der Aerosolgrößenverteilung von MDI gemäß Kaskadenimpaktor und Streulichtgerät Royco LAS 226

Comparison of aerosol size distributions of MDI according to cascade impactor and Royco LAS 226 light scattering.

R = Aerosol weight percentage made up by particles > d



Particle size

	Pressure of Propellant air Treibluft bar	Additional air Zuluft bar	liquid Material bar	°C	Concentration of Aerosol mg/m³
▽	10	1,2	10	80	353
△	10	1,2	10	50	294

Bild 16: MDJ - Aerosolverteilungen, 2 Schlick-Düsen mit Zyklon

MDI aerosol distributions. 2 Schlick nozzles with cyclone.

R = Aerosol weight percentage made up by particles > d

	Q m^3/h	3oo (1 mg/m^3)	2oo (1,5 mg/m^3)		1oo (3 mg/m^3)		5o (6 mg/m^3)	
		n	n	%	n	%		%
Kontron 2oo - 6	> 0,5 µm	o.r.			o.r.		o.r.	
	> 1 µm	3o			88	97	o.r.	
	> 2 µm	9			36	133	7o	13o
Royco 225	> 0,3 µm	361	463	86	759	7o	1994	92
	> 0,5 µm	195	26o	88	453	77	672	58
	> 0,7 µm	55	77	93	154	92	321	98
	> 1,4 µm	25	38	1oo	9o	12o	237	156
Royco 226	o,1 - o,17 µm	877	666	51	2oo	8	86	2
	o,17 - o,27 "	922	723	52	641	22	171	3
	o,27 - o,42 "	1o44	973	62	1165	5o	926	15
	o,42 - o,62 "	511	535	7o	929	6o	1179	38
	o,62 - o,87 "	396	446	74	879	73	13o6	54
	o,87 - 1,17 "	191	226	8o	54o	95	1o64	92
	1,17 - 1,52 "	96	115	8o	3o3	1oo	7o5	124
	1,52 - 1,92 "	24	28	78	87	12o	261	18o

Table 1: Substitute liquid -

Particle counts M = (x 10^3) at different aerosol concentrations.

o.r. = over range

Q = air flow through test rig.

d µm	c	n / 280 cm³	mg/m³	n / 280 cm³	mg/m³
0,3 - 0,5	0,4	946	0,12	361	0,05
0,5 - 0,7	0,6	543	0,23	195	0,09
0,7 - 1,4	1,0	190	0,35	55	0,12
1,4 - 2,0	1,7	121	1,12	26	0,23
> 2,0	2,0	0	0	0	0
Total mg/m³			1,82		0,49
Aerosol concentration by impactor mg/m³			2,3		0,8

Table 2: Substitute liquid

Comparison between the aerosol concentrations obtained with the Royco 225 (measuring volume 280 cm³) and the impactor

n = particle counts (x 10^3) at differentaerosol concentrations.

Date	Q m^3/h	t min	residence time in chamber min	Total aerosol deposit mg entry	exit	Concentration of aerosol mg/m^3 entry	exit
18.3.8o	loo	112	4,1	o,72	o,62	1,37	1,24
21.3.8o	66	15	6,o	4,oo	4,5o	6o,7	62,5
24.3.8o	loo	12o	4,1	2,1o	1,73	3,78	3,1o
28.3.8o	loo	12o	4,1	o,78	o,68	1,42	1,23
	loo	12o	4,1	o,91	o,47	1,65	o,85
1.4.8o	67	15	6,o	3,64	3,48	53,6	5o,7
	67	16	6,o	3,41	3,35	47,5	46,o
1o.4.8o	loo	5o	4,1	1,65	1,56	6,73	6,27

Q = air flow through test rig.

Table 3: MDI - Comparison of aerosol concentrations at entry and exit of the residence chamber. Gravimetric measurements - Cascade impactor.

Report Part B: Analytical Monitoring of Aerosols

List of Contents

Part B

Analytical Monitoring of Breathable Aerosols of Polymeric 4,4 - Diphenylmethane - Diisocyanate (MDI)

Author: Dr. P. Vogtel
Co-authors: Dr. A. Bürkholz
Dr. J. Keller

1. Analytical Plan

MDI aerosols in sizes ranging from o,3 - 3 µm and at concentrations between 1 mg/m^3 and 3 oo mg/m^3 were generated by atomization (see part A aerosol production). The monitoring and control of the aerosols took place purely physically by sampling using the cascade impactor and gravimetric analysis of the deposited masses.

The analysis which was carried out parallel to the necessary development work had two tasks. The first involved securing the gravimetricly determined concentrations by independent methods. On the one hand a procedure was developed which using the impactor as a sampling instrument enabled an analytical investigation parallel to the gravimetric determination of the material deposited on the impactor plates (infrared spectroscopy, determination of total carbon by combustion). On the other hand a method for the determination of the concentration independent from the cascade impactor and applying a direct sampling with related analysis (impinger washing bottle absorption, evacuated gas pipettes, sintered glass filters) had to be developed. Applying these techniques questions such as the dependency of stripping effects during the impactor sampling on concentrations and sampling times should be comparatively answered.

The second task involved an investigation of the chemical stability of the aerosol generated in order to confirm the identity of the aerosol inhaled with that of the material atomized. In addition to the quantitative assertions required to the present a set of complementary analytical methods was used to enable a qualitative description of the total MDI system.

The limits and possibilities of the individual methods are to be investigated and represented.

2. Characterization of MDI-survey of the analytic methods used.

MDI can be characterized by several typical parameters for which determination, different chemical and physical properties of the MDI material are made use of.

Three main parameters are regularly quantitatively determined.

2.1 Total content of isocyanate groups: titrimetrically by reaction with dibutylamine in chlorobenzene and back titration with HCl, results in % NCO (M=42)
typical value for MDI; 30 %.

2.2 Content of monomeric MDI and distribution of the MDI isomers, content of three nuclear component:
gaschromatographically (chromatogram see fig. 1).

2.3 Phenylisocyanate content: gaschromatographically (chromatogram see fig. 2), alternatively TLC or HPLC after derivatization using N-4-nitrobenzene-N-propylamine-Nitroreagent-(chromatogram see fig.3), typical concentration < 100 ppm w/w.
Further possibilities exist which besides determining single parameters allow collective properties of MDI to be measured as 'fingerprints'. These methods are arranged according to increasing qualitative characterizing information of the total isocyanate system.

2.4 UV spectroscopy: average value for the total aromatic system. (spectrum see fig. 4)

2.5 UV-VIS spectroscopy: dependent on the NCO content and position of the NCO-groups. NCO-groups are acidly hydrolysed, then diazotized and coupled (β-naphtol) and the corresponding azo-dyestuff photometrically determined (spectrum see fig. 5).

2.6 Thin-Layer-Chromatography - nitroreagent: MDI content and isomer distribution, fingerprint of the total MDI (chromatogram see fig.3).

2.7 High Pressure Liquid Chromatography - nitroreagent: MDI content, fingerprint of all isocyanates (chromatogram see fig. 6).

2.8 Exclusion chromatography: MDI content, MDI oligomers arranged according to molecular weight (chromatogram see fig. 7).

2.9 IR spectroscopy: NCO content, fingerprint of the total MDI, specific information on the following groupings:

-NCO isocyanate	2270 - 2240 cm^{-1}
-N=C=N- carbodiimide	2140 - 2120 "
-C=O in the uretdione ring	1780 - 1760 "
in esters	1750 - 1720 "
in urethanes	1720 - 1700 "
in the uretonimine ring	1720 - 1710 "
in allophanates and biurets	1730 - 1700 "
in ureas	1660 - 1640 "
-C-N- in the isocyanurate ring	1420 - 1405 "
in the uretdione ring	1385 - 1375 "
in the uretonimine ring	1380 - 1360 "

(spectrum see fig. 8 - film -, fig. 9 - solution in CCl_4)

3. Quantitative Measurements of the Aerosol

3.1 Sampling using the cascade impactor

The cascade impactor was set up as the sampling instrument for the control of the aerosol concentration. The determination took place by weighing the masses deposited on the impactor platelets. This method for the determination of concentration is, however, unspecific. In order to exclude the possibility of error the gravimetric analysis should therefore be further analytically supported. Infrared spectroscopy was the method chosen (see 2.9). These measurements were made at low (5 mg/m^3) and intermediate (5 to 100 mg/m^3) concentrations. After weighing the platelets with the deposited MDI they were washed and reweighed. In the CCl_4 solution a quantitative determination of MDI was carried out and the values correlated.

Table 1 shows for example some of the results obtained in this way, in which knowledge and experience gained from previous experiments found application.
For concentrations above about 5 mg/m^3 the analytically and gravimetricly determined values agree to within 2o % of each other. For smaller concentrations the deviation increases up to 5o %.
The relative increase in the deviation can be explained by errors which are constant and independent of the aerosol concentration. The errors are made in the determination of the absolute masses of the material deposited on the platelets by weighing them or by determining the MDI in the CCl_4 solution. For an impactor series (1o platelets) differences of o.o6 to o.6 mg of MDI absolute between gravimetric and IR analysis are to be expected.
This is caused by weighing errors, analytical errors and reduced findings due to partial reaction of the MDI on the glass platelets. These lead to 1o % derivation at intermediate concentrations (measurement on 3/5/8o (6,7 resp. 6,1 mg), and 5o % at lower concentrations (o,7 resp. o,33 mg) for the measurement on 3/3/8o).

This is outlined by table 2 which shows the results of two measurements at different aerosol concentrations. To give a better impression the results are divided into 3 groups.
A further confirmation is provided by additional experiments in which MDI was directly deposited on the glass platelets, then after different standing times (simulation of different sampling times) dissolved in CCl_4, followed by quantitative MDI-determination by IR-analysis. An influence of the standing time and of the absolute masses deposited has not been found. The differences in the absolute amount of MDI by gravimetry and analysis are of the same order of magnitude as in the previous investigations, table 3 a.

Weight increases by water uptake which would have been conceivable could not be established.

It can be concluded from the independence of the absolute differences (mg) between gravimetry and analysis from aerosol concentrations and to a certain degree from the sampling times that the aerosol after being deposited onto glass platelets remains to a great extent unchanged. The differences just mentioned are caused by the working method chosen (weighing differences, dissolving off

from the glass platelets, interactions with the glass surface).

An additional assurance of the analysis took place by carrying out a second analytical determination in which the material deposited on the glass platelets was burned in a Wösthoff apparatus; the total carbon content determined and expressed in terms of MDI.

Interference due to foreign dust particles (organic or inorganic) can be detected in this way; weighing errors being excluded. The results for two series of readings (low and intermediate concentrations) are summarized in table 3 b. The agreement between the analysis lies also here in the same range as the measurement precision (0,2 to 0,5 mg absolute derivation per impactor series) in this way confirming also the IR analysis and the gravimetric results.
The impactor method coupled with gravimetry can therefore be applied within the above mentioned error limits for the monitoring of aerosol concentrations. It should also be noted, however, that the time and work to be spent is considerable. A repeated analytical assurance in the manner described is necessary, in order to exclude errors due to external influences (dust, smut).

3.2 Direct sampling

Sampling using a cascade impactor is indirect, as first of all a deposition takes place and secondly a transferoperation is necessary for the determination of the deposited material (dissolving off of the sample before reweighing in the case of gravimetry, dissolving in CCl_4 for the IR analysis). During the sampling the sample is exposed unprotected to the surrounding air. In the case of direct sampling (washing bottle absorption with different solvents, with and without derivatization, gas pipette sampling, sampling with sintered glass filters) difficult error-causing transfer operations nor longer exist. The samples are protected in solution and/or by derivatization. Chemical changes during the sampling process are either not or extremely limitedly possible. In the case of substances capable of undergoing a reaction the direct sampling can therefore be said to impart more and better information than that which is possible by indirect sampling. Problems of sample volatility no longer exist.

For this reason direct sampling was carried out in a series of tests parallel to the cascade impactor measurements. This proceeded with

- Midget impinger washing bottles manufactured by the Bendix Company and personal air sampling pumps of the same manufacturer (flow rate 2 l/min) the following found application as absorption liquids:
  a) toluene/nitroreagent (s. 2.6)
  b) CCl_4 (s. 2.9)
  c) H_2SO_4/Dimethylsulfoxide (DMSO) (s. 2.5)

- Evacuated 5 l gaspipettes washed out immediately after sampling with 25 ml toluene/nitroreagent solution.

- G 4 sintered glass filters (pore size 1o to 2o µm, manufactured by Schott, Mainz).

The results are summarized in table 4.
Concentration values obtained by direct sampling lie significantly lower than the values obtained using a cascade impactor. For intermediate concentrations 7o - 8o % of the gravimetrically determined quantities are still found. For concentrations under 3o mg/m^3, however, agreement between results falls below 2o % to 1o %.

The analytical methods (IR,UV,HPLC,TLC) were checked one against the other and confirmed each other (see e.g. table 5). The reduced findings can therefore be said to be substantiated by the sampling system. Sampling with impinger washing bottles is normally applied for gases or substances which due to their partial pressure are in the gaseous state. As is generally known the effectiveness of such systems for aerosols is a function of the particle size; it decreases with decreasing particle size.
This is caused in the unfavourable relation between surface and volume of the small particles and in the high surface energy which must be overcome by absorption.

The examined aerosols lie in the range of particle sizes between o,3 to 3 um. The maximum particle size shifts within this range with the total aerosol concentration (see Part A, fig. 14 and 16). At concentrations around 2 mg/m^3 only 2o % of the particles are

larger than 1,5 µm and at concentrations between 100 to 300 mg/m^3 60 - 80 %.

Taking this into consideration a critical threshold value for the range of droplet sizes 1 to 2 µm seems to exist which plays a part in deciding the effectiveness of the applied washing bottle system. This explains the somewhat more acceptable effectiveness at higher aerosol concentrations and the poor effectiveness at low concentrations with an associated higher fraction of particles <1 µm.

The concentration control of aerosols independent of the cascade impactor which was a task of the direct sampling could therefore not be achieved.
In this case other methods must be found. These are discussed later. The question whether with the cascade impactor a stripping effect of the deposited MDI takes place, can therefore not be answered with confidence (see chapter 3.1).

A second task, study of the chemical stability of the aerosols by means of direct sampling is possible in the range of intermediate aerosol concentrations. Knowledge gained from this study can be applied to lower concentrations (see remarks on the droplet size distribution on fig. 14 and 16, Part A).

4. Measurements at Entry and Exit of the Residence Chamber

In the previous measurements the aerosols remained only a few seconds in the surrounding air before sampling. In the inhalation chamber for the animal experiment the mean residence time (calculated from chamber volume/total quantity of air) amounts to two minutes. In order to simulate these conditions a residence chamber (6,8 m^3) with entry and exit was additionally built in. Samples were taken from the chamber entry and exit with the cascade impactor and directly using impinger-washing bottles.

4.1 Impactor measurements

see Part A, 5.2.2

The analytical values in table 7 are arranged in comparison to the gravimetric values from part A, table 3 according to falling concentrations. The analytically determinable fraction in % of the gravimetric value is also given. Also in this case as already discussed in chapter 3, the agreement for values over 2 mg/m^3 is satisfactory. At lower concentrations it decreases considerably.

4.2 Direct Sampling

Samples were taken parallel to the impactor measurements at intermediate and low concentrations. Here 3 absorption systems with the relevant analysis found application:
toluene/nitroreagent followed by TLC, H_2SO_4/DMSO followed by photometry, CCl_4 followed by IR analysis.

The analytical findings confirmed one another in this way.
The results are found in table 7. They are at intermediate concentrations in tolerable agreement. The decrease in the aerosol concentration established by sampling is larger (decrease 2o %) than that established by using the cascade impactor (≦ 8 %).
At lower concentrations the direct sampling failed. Assertions on the correlation of values established using the cascade impactor are therefore not possible.

5. Aerosol stability

In the previous measurements the quantitative aspect for monitoring total aerosol concentration was the main point of consideration. By carrying out measurements enabling a qualitative statement on the aerosol composition it should be additionally ascertained that the MDI undergoes no changes during the time it spends in the air. For the Toxicological investigations this second step ensures that the inhaled material is identical to that having been atomized. For this experiment a direct sampling is necessary in order to exclude changes after the deposition. With reasonable effectiveness this is only applicable at intermediate concentrations. As the width of the droplet size sitribution (o,3 to 3 µm) at high and low concentration is identical (only the centre of gravity shifts within the distribution) an extrapolation to lower values is allowed although a further supporting analysis should be made in future.

5.1 Information content of the analytical techniques

MDI is a complex mixture of monomeric and oligomeric isocyanates. The qualitative and quantitative description of such a mixture using a single analytical process is not possible. Three procedures were therefore combined and specific individual investigations applied. These provided besides specific information in each case a "fingerprint" of the total system from which different supplementary information could be gained.

IR spectroscopy (s. fig. 8,9) shows NCO-bands as a direct measure for the stability of the isocyanate group and besides the typical skeletal vibration pattern a number of characteristic single bonds, which are also specified and to which typical reactions of the isocyanate-groups, eq. urea formation (-C=O in ureas 1660 - 1640 cm^{-1}) can be attributed. Besides showing the content of MDI 4,4 exclusion chromatography shows the typical oligomer and polymer distribution arranged according to increasing molecular weight. Changes due to oligomerization can be specifically identified.

TLC or HPLC after derivatisation (s. fig. 3) show besides the content of MDI 4,4 and the distribution of its oligomers also a specific fingerprint. In this fingerprint it is only possible to a limited extend to identify single species, but changes of the whole system which will cause additional spots in the chromatogram to arise can be observed with high sensitivity.

The aerosol can be tested for PhI and aromatic amines (eg. MDA 4,4; see fig. 1c) using thin-layer-chromatography after derivatisations. Together with the examination of the residue remaining in the cyclone the question of whether an enchrichment of PhI in the aerosol has taken place can in this way be answered. Great care must be taken in the testing for aromatic amines in order to avoid false interpretations which can arise due to the in situ-formation of aromatic amines on the TLC plates (acid decomposition by silicagel).

5.2 Analytical Investigations

Along with the methods described in 5.1 aerosol measurements were carried out with and without the residence chamber. The residence times of the aerosol in the carrier-gas system were of the

order of several seconds to 2 minutes. The sampling times were approximately 15 minutes.

Identical results were found for all the investigations. Only results obtained by measurements using residence chambers are explicitly represented (general conditions see table 7 and Part A, table 3).

5.2.1 The PhI concentrations in MDI which was applied for atomization agree with those of the MDI deposited in the cyclone (GC, <1oo ppm w/w). No PhI is detectable in the aerosol for the given sampling times & volumes (TLC, detection limit o,oo2 ppm v/v, see fig. 3).+) Therefore no measurable PhI enrichment in the aerosol occured.

5.2.2 The test for aromatic amines (eg.MDA 4,4, Aniline) were negative, detection limit o,oo2 ppm v/v. Indication of hydrolysis reactions are not given by this test.

5.2.3 The comparison of the TLC-nitroreagent-fingerprints showed no difference between the atomized MDI, the portion deposited in the cyclone and the aerosol. (see fig. 3). Indications of hydrolysis, oligomerization or rearrangements are not given by this test.

5.2.4 Exclusion Chromatography: After sampling in CH_2Cl_2 the applied MDI, the portion of MDI deposited in the cyclone and the aerosol itself indicated the same distribution of oligomers and polymers (see fig. 11). Indications of oligomerisation are not given by this test.

5.2.5 IR-Spectroscopy: After sampling in CCl_4 or with the impactor and removal of the solvent in a vacuum KBr pellets were produced. Spectra of the starting material (fig. 12), of the portion deposited in cyclone (fig. 13) and of the aerosol (fig. 14) were recorded. These spectra give no indication of chemical changes, they are identical within the degree of measurement precision.

+)Total air volume 50 litres.

In order to substantiate the informative strength of the spectra fig. 15 shows in comparison with the above the IR spectrum of a MDI sample deposited on a glass plate, which was left open to the laboratory air over night. Here chemical changes at 2800 cm^{-1} (aliphatic) and at approximately 1700 cm^{-1} are clearly seen.

6. Conclusion and outstanding problems

Analytical measurements were carried out on aerosols in sizes ranging from 0,3 - 3 µm at concentrations between 1 mg/m^3 and 100 mg/m^3. For these measurements a conventional direct sampling technique (impinger-washing-bottles, evacuated gas-pipettes, G4 glass-sintered filters) and sampling using a cascade impactor was applied. The evaluation of the impactor measurements was carried out physically by weighing the deposited masses and analytically by dissolving them in CCl_4 followed by quantitative determination of MDI by means of the NCO band. An assurance of the values obtaines above was provided by combustion of the deposited masses in a Wösthoff apparatus and determination of the total carbon content. According to this method agreements of 80 % were reached at intermediate concentrations falling to 30 % at low concentrations.

By means of additional experiments the decreasing agreement could be traced back to constant concentration - independent errors caused by the working method chosen. The chosen procedure is basically not limited by this. The cascade impactor is therefore satisfactory as a sampling instrument for the monitoring of low and intermediate MDI concentration within the error range described above providing a supporting analysis excludes errors due to external factors (eg. dust). The time and work expenditure along with the qualification of the personnel should also be taken into consideration.

The effectiveness of the conventional sampling procedure shows large fluctuations (10 - 90 %) for the aerosols described. These fluctuations can possibly be traced back to shifts of the centre of gravity of the particle size distribution within the 0,3 - 3 µm spectrum (eg. shifting of the centre of gravity from 0,8 µm at 1 mg/m^3 to 1,6 µm at 50 mg/m^3).

According to this the critical threshold limit which determines the effectiveness of conventional sampling systems seems to lie between 1 - 2 µm for the aerosols of the type investigated. Therefore the comparitive investigations between direct sampling and cascade impactor which are of special interest at low concentrations produced no results.
A stripping effect due to the volatility of the MDI deposited on the glass-plates would influence both gravimetry and analysis as a function of the aerosol concentration (at decreasing concentration ≙ reduced amount of deposited masses longer sampling times are necessary). The question whether such an effect exists cannot be answered with total confidence. For the same reason a simple and more reliable procedure for monitoring of aerosols of the concentration level can presently not be offered.

Additional experiments are necessary. These should first of all include investigation of the volatility of MDI deposited on the glass plates as a function of the quantity of gas passed over them. Secondly suitable sampling procedures for aerosols of the kind described must be developed. For this purpose a tubular sampling with impregnated stationary phase or an impregnated glass wool is contemplated.

The investigation of the chemical stability was performed at concentrations $\geq$ 10 mg/m^3 both with and without the residence chamber. It involved the combined application of exclusion chromatography, IR spectroscopy and TLC along with HPLC after derivatization of the isocyanate groups. In addition the PhI enrichment in the aerosol and formation of aromatic amines was specifically tested. A PhI enrichment in the aerosol was not observed (detection limit 0,002 ppm v/v). No formation of aromatic amines (MDA, Anilin) was established (detection limit 0,002 ppm v/v). The combined investigations using TLC, HPLC, GPC and IR showed no changes between the aerosol the starting material and the portion of it deposited in the cyclone.

It can be concluded from this that the aerosol over its residence in the gas phase remains (during 2 minutes) chemically within the range of measurement precision.

After presenting suitable direct sampling techniques supplementary experiments at the 1 mg concentration level are recommended for completion of the investigations. These studies should be subject of a new contract.

Tabelle 1:

Sampling with the cascade impactor: comparison of gravimetry and IR-Analysis

Date	air-stream Q [m^3/h]	sampling time t [min]	Aerosol absolute [mg] gravimetr.	analytical	Aerosolconcentr. [mg/m^3] gravimetr.	analytical
3. 3.80	100	60	0,7	0,33	2,5	1,15
	100	60	1,04	0,4	3,7	1,38
4. 3.80	62	62	1,5	1,3	5,0	4,3
	62	62	2,2	1,6	8,1	5,9
5. 3.80	66	15	6,7	6,1	94	85
10. 3.80	100	30	1,15	1,1	8,2	7,8
	100	120	0,34	0,17	0,6	0,3

Tabelle 2:

Comparison of gravimetry and IR-Analysis by absolute values [mg]

Date	gravimetry [mg]	analysis (IR)	Fraction
3.3.80	1,03	0,83	0,3 - 1 µm
	0,43	0,41	1 - 3 µm
	1,48	1,44	3 µm
	2,23	1,94	0,3 - 1 µm
	3,21	2,92	1 - 3 µm
	1,28	1,15	3 µm

Tabelle 3 a: Test of solubility of MDI after deposition on glass-plate

Date	gravimetry [mg]	analysis	Time of deposition [min]
30.11.79	4,2	4,0	0
	3,13	3,5	5
	4,8	3,5	30
	4,1	3,5	1000

Tabelle 3 b: Checking of gravimetry-Ir-Analysis by means of the TOC-value (combustion)

Concentrations	Impactor 1 grav.	anal.	Impactor 2 grav.	anal.	Impactor 3 TOC ,Combustion
MDI [mg/m³]	53,6	49,0	47,5	40	66,4
	50,7	46,0	46	38	39,4
	1,42	0,56	1,65	0,54	1,04
	1,23	0,49	0,95	0,54	0,63

Tabelle 4:

Sampling with cascade impactor, compared to direct sampling.

Date	mg MDI/m³ Impactor Gravimetry	IR	Impinger-washing-bottles Toluene/NR	CCl_4	H_2SO_4/DMSO	evacuated gas pipettes 5l	Glass-sintered filters G 4
7.12.79	121	102	78	-	-	-	-
	118	88	78	-	-	-	-
22.10.79	54.8	-	12.5	-	-	18.5	17.5
1. 4.80	53.6	49.0	45	37	48.5	-	-
	50.7	46.0	35	31	38.6	-	-
22.11.79	34	-	4.5	4.2	3.5	-	3.0
16. 1.80	31.4	13.0	6.5	4.0	-	-	5.8
	31.7	6.4	-	-	-	-	-
27. 3.80	1.42	0.56	0.13	0.15	<0.2	-	<0.01
	1.23	0.43	0.08	0.10	<0.2	-	<0.01

Tabelle 5a:

Comparison of different methods of analysis

Date	Sampling: impinger-washing-bottles with	Method	Result mg MDI/m^3
22.11.79	Toluene/Nitroreagent	DC	4.5
"	"	HFC	4,0
"	CH_2Cl_2	UV, 281 nm	4,6
		236 nm	4,2
"	H_2SO_4/DMSO	Photometr.	3,5
"	CCl_4	IR	4,2

Tabelle 5b:

Comparison of methods by means of samples from the glass-plates of an cascade impactor (directly after sampling, samples 0.05 % nitroreagent in toluene).

glass-plate Nr.	Particle size µm	HPLC µg/plate grav.	HPLC mg/m^3 MDI	TLC µg/plate grav.	TLC mg/m^3 MDI
2	0,47	0,17	0,10	n.n.	0,00
2a	0,70	2.3	1,25	1	0,55
3	1,1	5,5	3,00	4	2.15
4	1,7	7,2	3,87	7	3.80
5	2,5	7,7	4,13	8	4,33
6	3,4	1,6	0,88	2	1,07
7	4,3	1,4	0,75	1,5	0,82
8	5,7	2,0	1,07	1,5	0,82
8a	7,7	0,5	0,25	1	0,55
9	12,5	0,16	0,10	0,5	0,28
10	17	0,1	0,00	n.n.	0,00
	Σ	28,5	15,4	26,5	14,4

Tabelle 6:

Measurements with the cascade impactor at entry and exit of the residence chamber with intermediate and low concentrations [in ( ), values at exit]

Date	Q [m^3/h]	t [min]	Residence time [min]	Aerosol absolut mg gravim.	Aerosol absolut mg analytical	Aerosolconcentration [mg/m^3] gravim.	Aerosolconcentration [mg/m^3] anal. MDI
18.3.80	100	112	4,1	0,72 (0.62)	0,33 (0,30)	1,37 (1,24)	0,63 (0,57)
21.3.80	66	15	6,0	4,00 (4,50)	3,10 (3,78)	60,7 (62,5)	47,0 (54,2)
24.3.80	100	120	4,1	2,10 (1,73)	0,96 (1,10)	3,78 (3,10)	1,74 (1,79)
28.3.80	100	120	4,1	0,78 (0,68)	0,30 (0,27)	1,42 (1,23)	0,56 (0,49)
	100	120	4,1	0,91 (0,47)	0,30 (0,30)	1,65 (0,85)	0,54 (0,54)
1.4.80	67	15	6,0	3,64 (3,48)	3,33 (3,16)	53,6 (50,7)	49,0 (46,0)
	67	16	6,0	3,41 (3,35)	2,80 (2,70)	47,5 (46,0)	40,0 (38,0)
10.4.80	100	50	4,1	1,65 (1,56)	1,31 (1,25)	6,73 (6,27)	5,34 (5,02)

Tabelle 7:

Comparison gravimetry-IR-Analysis by sampling with cascade impactor at the residence chamber

Concentrations $[mg/m^3]$			sampling time
gravimetry	Analysis (IR)	%	t (min)
60	50	83	15
52,5	47,5	90	15
47	39	83	16
5,6	5,2	93	50
2,1	1,8	85	120
1,1	0,5	46	120
1,1	0,5	46	120
0,97	0,60	62	112

Tabelle 8: Comparison of direct sampling with the cascade impactor by measurement at entry and exit of the residence chamber at intermediate and low concentrations.

	impinger-washing-bottles [mg/m³]			Impactor 1 [mg/m³]		Impactor 2 [mg/m³]	
	Toluene/NR	$DMSO/H_2SO_4$	CCl_4	grav.	anal.(IR)	grav.	anal.(IR)
entry) r.chamber	45	48	37	53.6	49.0	47.5	40
exit)	35	39	31	50.7	46.0	46.0	38
entry) r. chamber	0.13	<0.2	0.15	1.42	0.56	1.65	0.54
exit)	0.08	<0.2	0.10	1.42	0.49	0.85	0.54

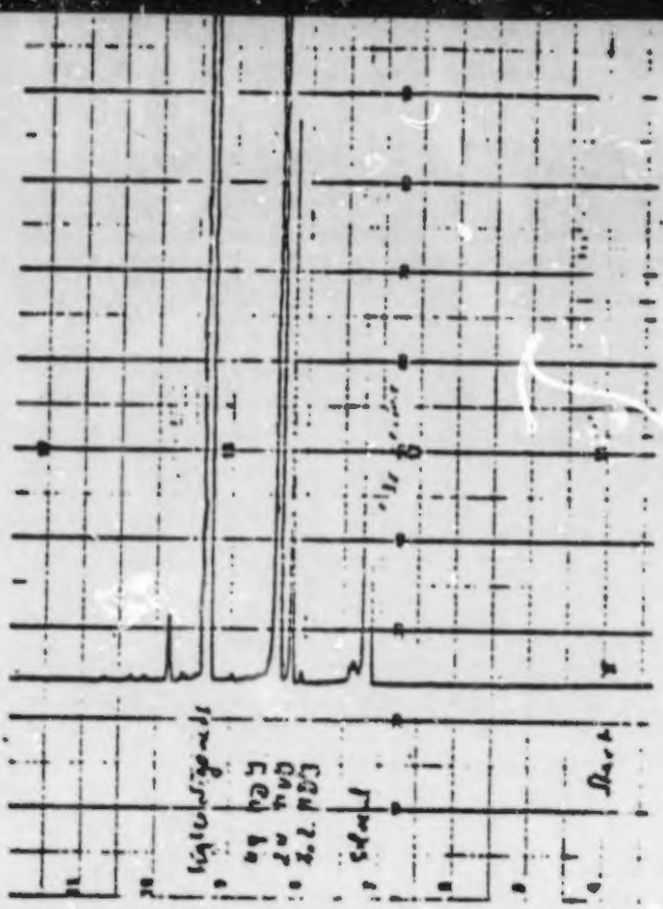


Figure 1: GC-Chromatogram of MDI 4.4. and its oligomers

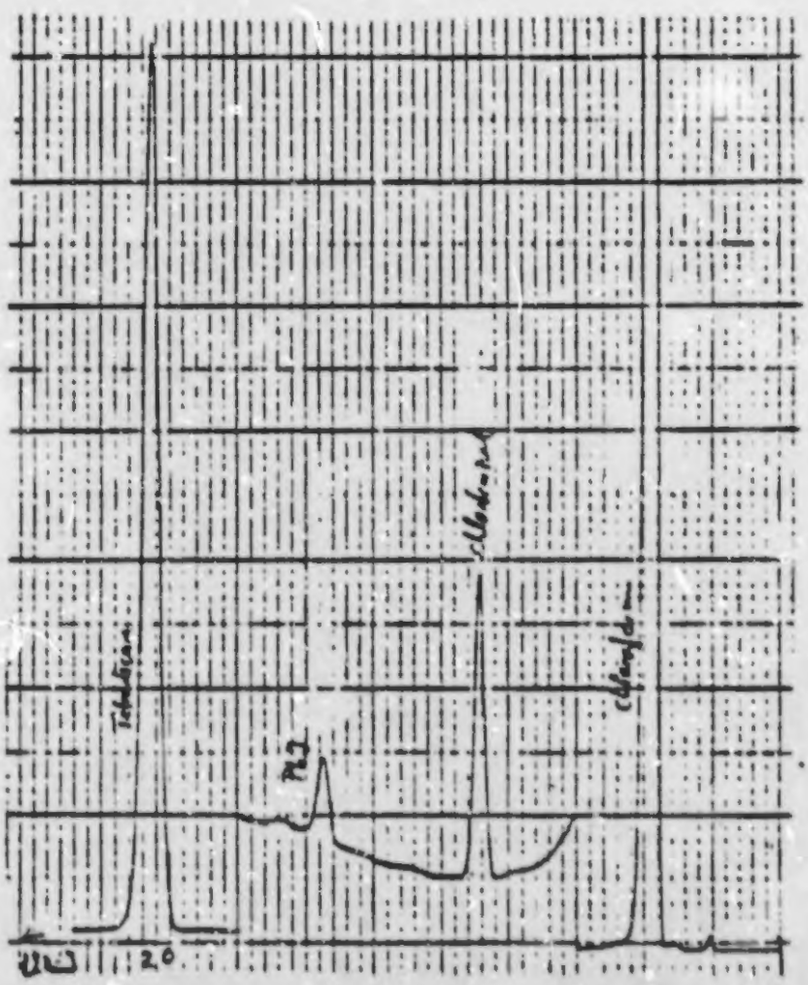


Figure 2: GC-Chromatogram of PhI in MDI

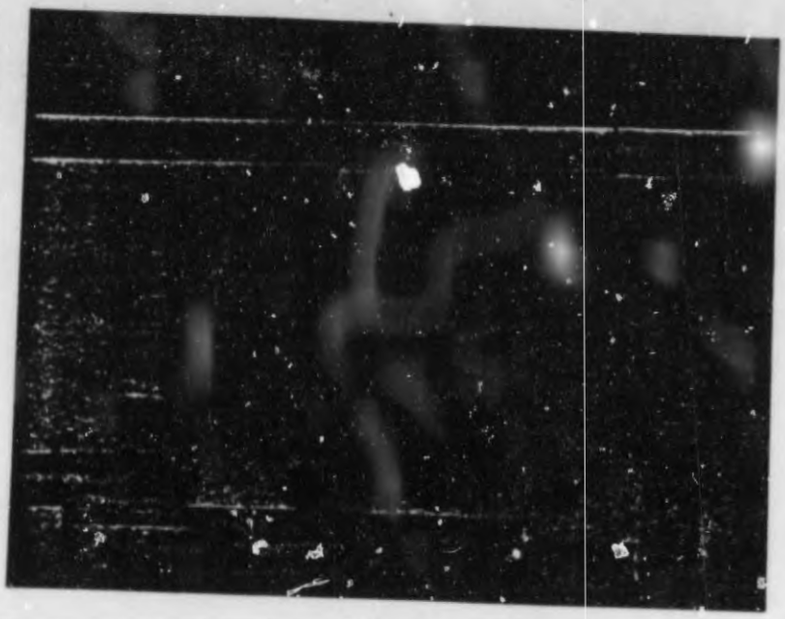


Figure 3: TLC-Chromatogram: PhI and fingerprint of MDI

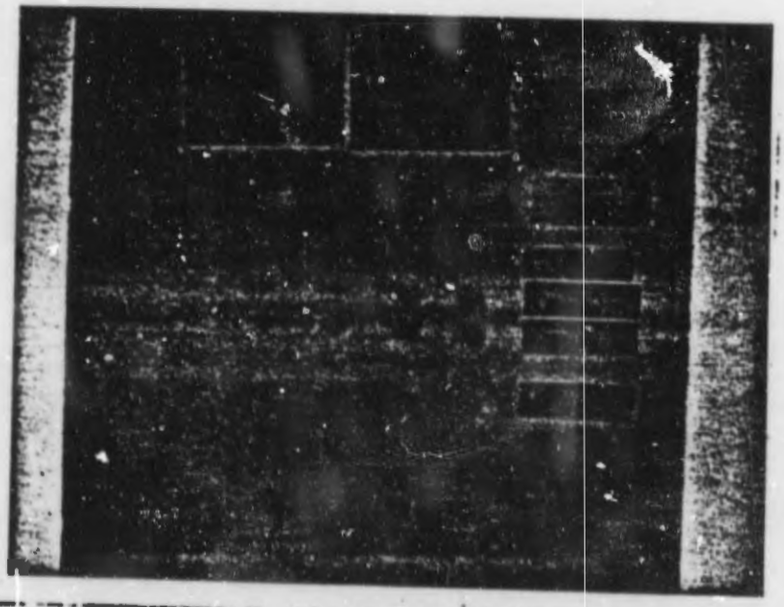


Figure 10: TLC-Chromatogram: Separation of aromatic Amines

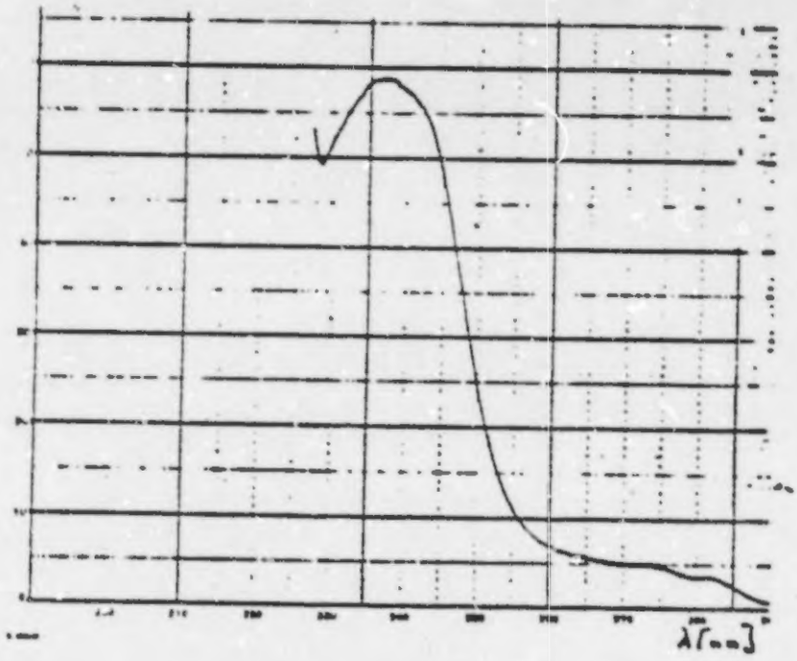


Figure 4: UV-Spektrum of MDI

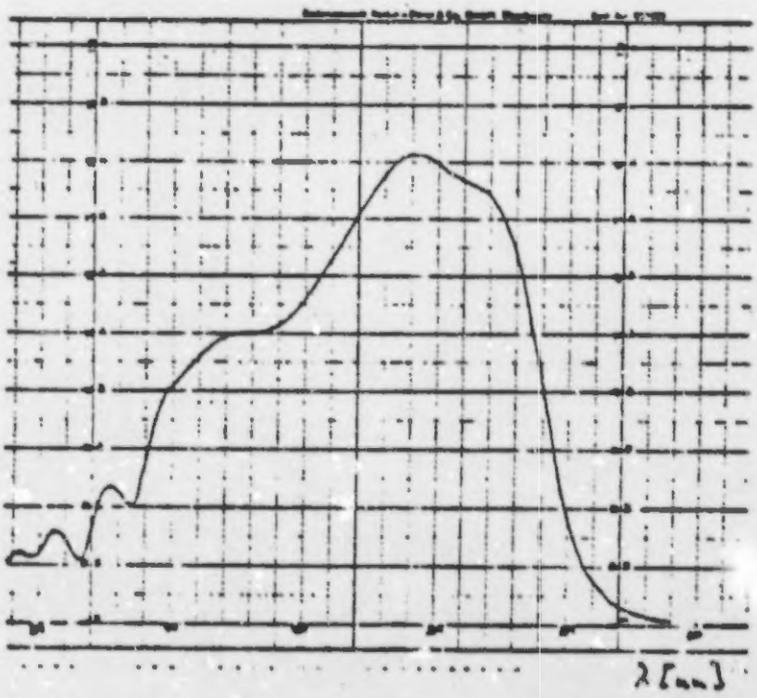


Figure 5: UV-VIS-Spectrum of MDI-Azo-dye

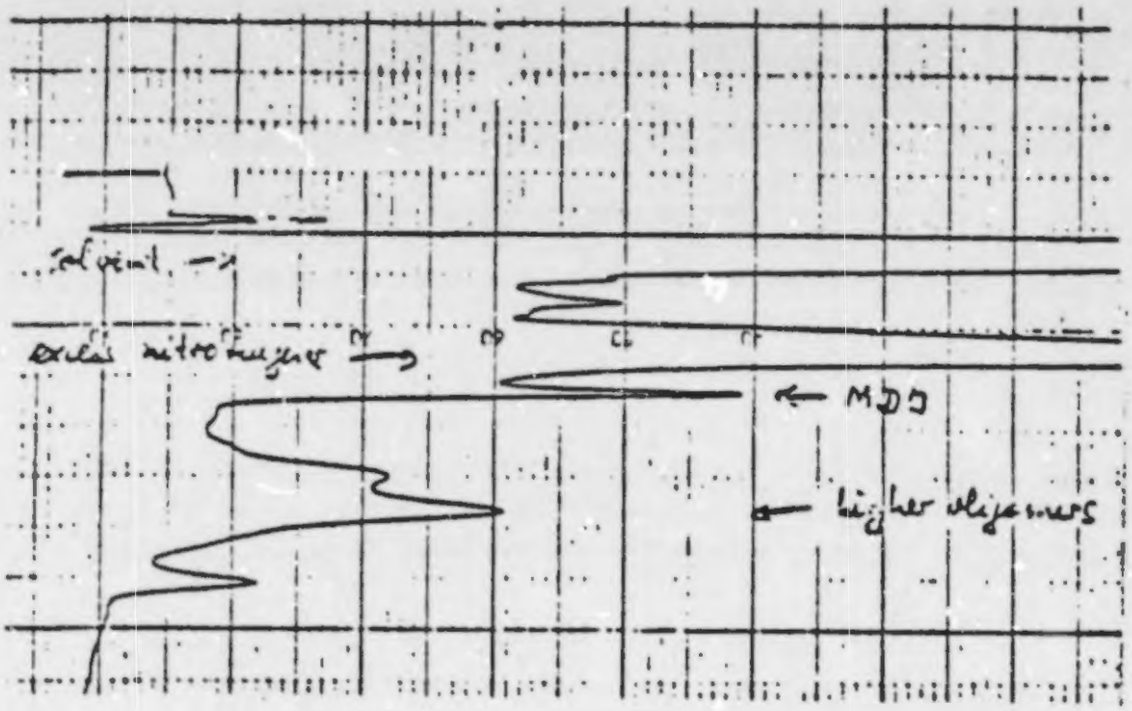


Figure 6: HPLC-Chromatogram of MDI

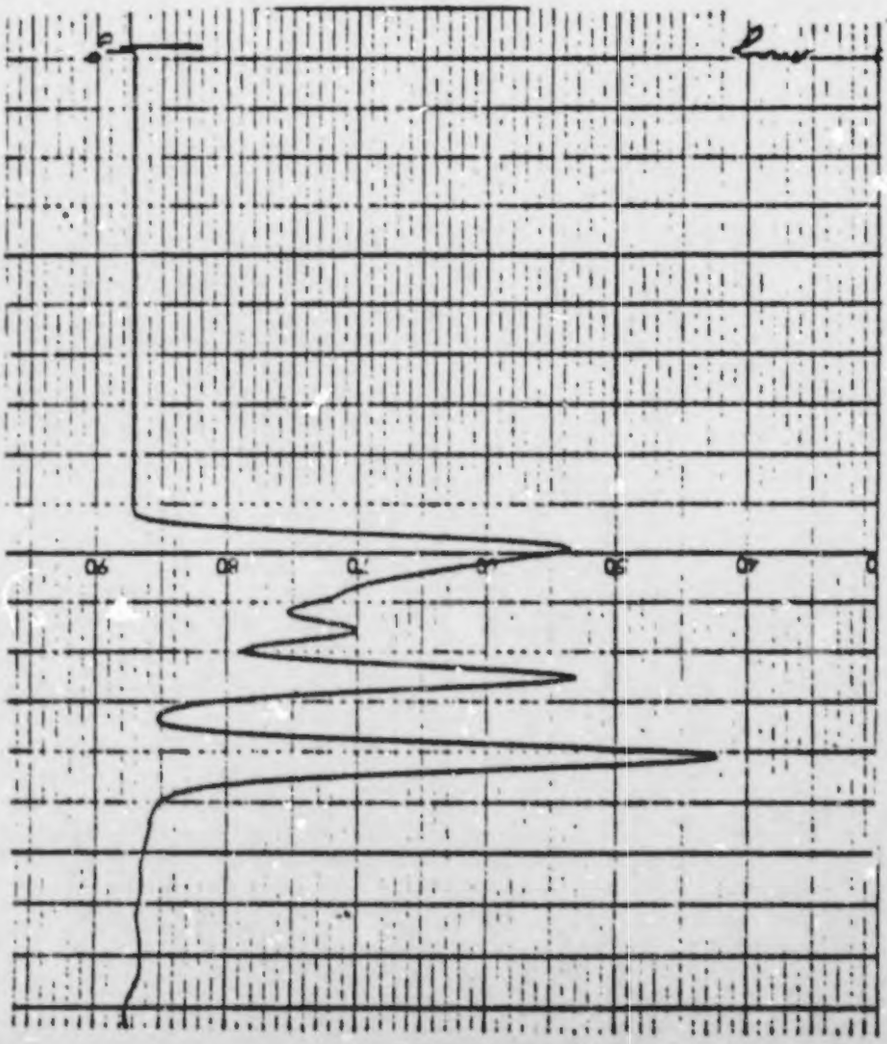


Figure 7: GPC-Chromatogram of MDI

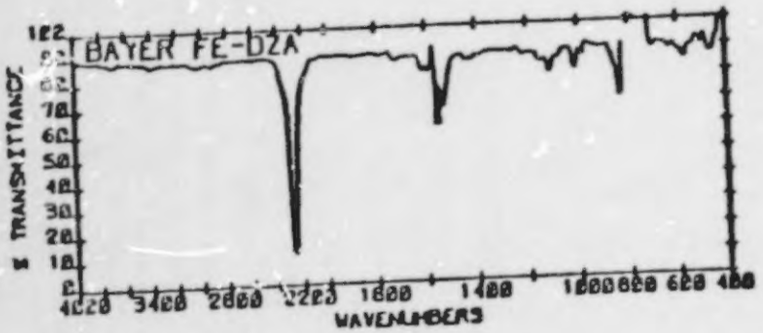


Figure 8: IR-Spektrum of MDI in CCl_4-solution

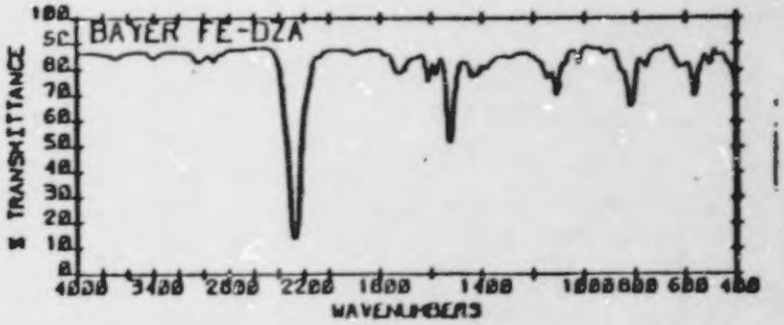


Figure 9: IR-Spectrum of MDI as film

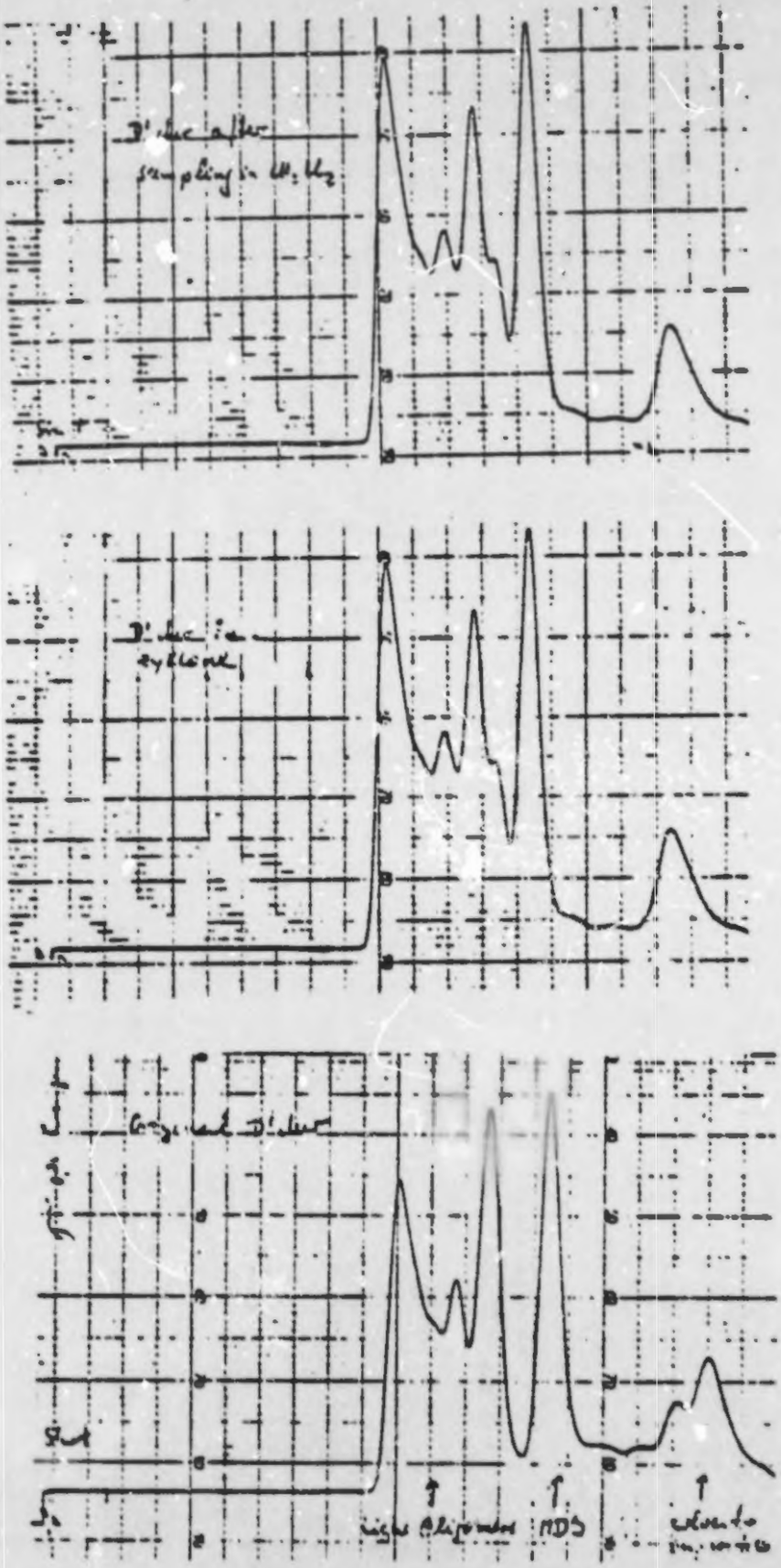


Figure 11: Comparison of MDI by GPC:
Original material, residue in cyclone, aerosol

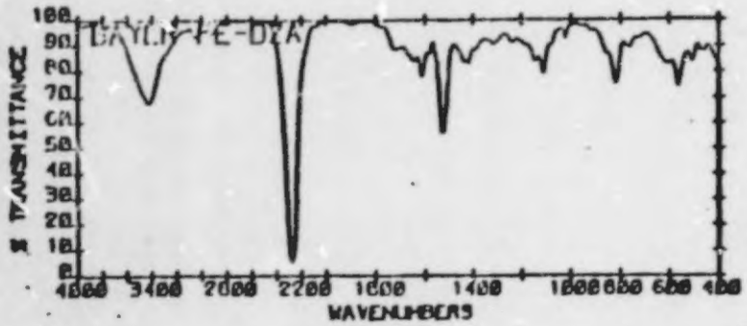


Figure 12: IR-Spectrum of original MDI, KBr-pellet

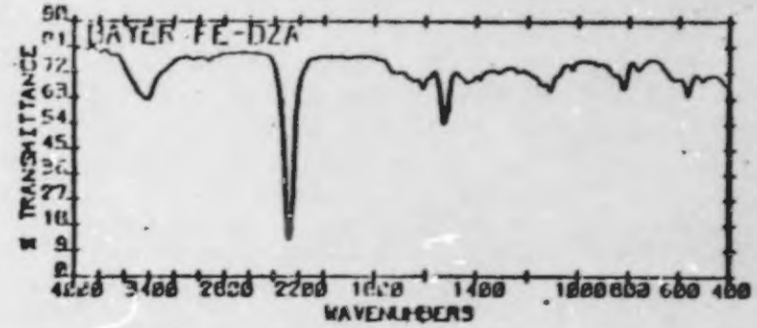
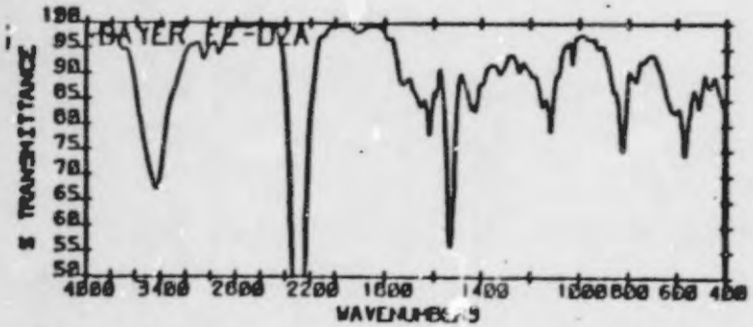
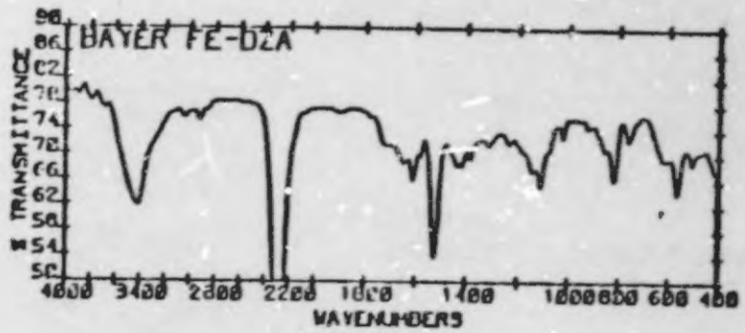


Figure 13: IR-Spectrum of the residue in cyclone, KBr-pellet





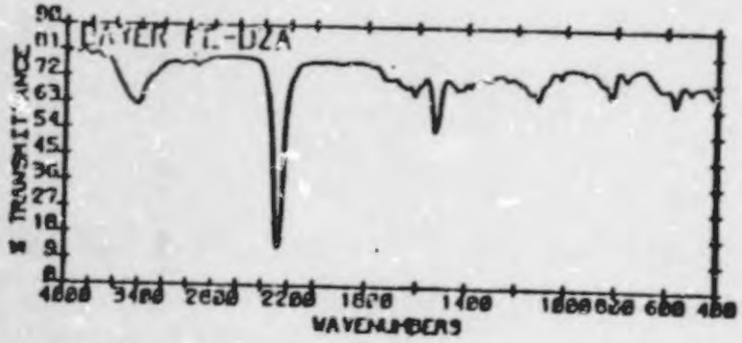
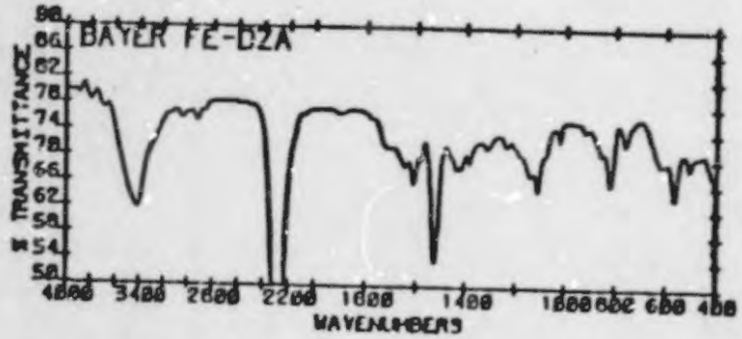
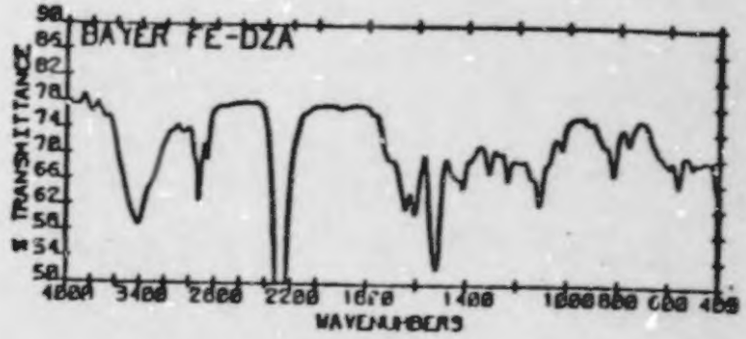


Figure 14: IR-Spectrum of the aerosol, KBr-pellet

Figure 15: IR-Spectrum of material after deposit on glass-plates and storage over night, KBr-pellet





CERTIFICATE OF AUTHENTICITY

THIS IS TO CERTIFY that the microimages appearing on this microfiche are accurate and complete reproductions of the records of U.S. Environmental Protection Agency documents as delivered in the regular course of business for microfilming.

Data produced 11 (Month) 10 (Day) 88 (Year) Barbara Smith Camera Operator

Place Syracuse (City) New York (State)

AMTEK corp